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ARCHIVES OF SURGERY

VOLUME 23 AUGUST, 1931 NUMBER 2

GALLSTONES IN THE COMMON BILE DUCT *

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Calculous disease of the biliary system is a condition frequently encountered by the surgeon. Treatment for cholecystitis, with stones, is now a relatively easy surgical problem, and is usually followed by a result that is satisfactory to the patient. However, when the bile ducts become involved either by the passage of stones from the gallbladder into the ducts or by the formation of stones within the ducts themselves, the problem becomes more serious, both for the patient and for the surgeon.

We have recently reviewed a series of 1,608 consecutive cases in which stones of the common bile duct were removed by operation at the Mayo Clinic. This number does not include 160 cases of stones in the ampulla of Vater that we have reported elsewhere. The 1,768 patients who underwent removal of stones from the common bile duct, including the ampulla of Vater, represent 13.2 per cent of all those from whom gallstones were removed during the period corresponding with that during which the cases included in this study were collected. There were 1,120 women and 488 men in this series, a ratio of 2.2 to 1.

The distribution in various groups according to age is interesting. The youngest patient was 5 months, and a fourth of the patients were more than 60 years. It is of interest to note that, on an average, the female patients came for surgical intervention five and a half years earlier than the males.

SYMPTOMS AND DIAGNOSIS

In the diagnosis of stone in the common bile duct, a complete history usually offers the most useful clue, in spite of recent laboratory aids and diagnostic refinements. The most characteristic feature of stone in the common bile duct is the intermittent nature of the symptoms.

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* Read before the Inter-State Post-Graduate Medical Association, Minneapolis, Oct. 20-24, 1930.

Many years ago, Osler described the typical symptoms of stone in the common bile duct as paroxysms of colicky pain, chills and fever and jaundice, followed by periods of comparative or complete freedom from symptoms. Most patients with stones in the common bile duct present a history of intermittent trouble, although any one or all of the symptoms may be lacking. It is well known that stones in the common bile duct may lie dormant for months or years and apparently cause no symptoms. Sooner or later, however, in most cases there is irritation of the mucous lining of the ducts, which produces an inflammatory reaction with edema around the stone, occluding the duct, and giving rise to biliary obstruction. If infection is present, symptoms of sepsis appear, and if the obstruction is more or less complete, jaundice becomes evident. In most cases these acute symptoms last only a few hours or a few days, and then the attack is over, leaving only residual soreness in the right upper quadrant of the abdomen. But as time goes on the attacks become more and more frequent, with less complete relief in the intervals, so that there is hardly time for recovery from one attack before another one appears.

Pain is the most common and most characteristic symptom of stone in the common bile duct. This usually is of the typical colicky type. In our series of 1,608 patients, 1,293 (80 per cent) had a definite history of one or more attacks of severe, biliary colic which usually required an opiate for relief; 275 (17.1 per cent) complained of pain in the epigastrium, variously called dull, boring or aching, but not sufficiently severe to be classified as colic, and in 40 (2.4 per cent) no pain occurred at any time in the course of the disease.

Jaundice was present in 1,181 (73.4 per cent) of the cases. In 1,105, the jaundice was of the intermittent type, coming in paroxysms, with intervals of complete freedom. In 76, the jaundice was persistent from its onset, but usually varied in degree. Of the 1,181 patients who had jaundice it was present at the time of admission to the clinic in 222 (18.8 per cent). In 427 (26.5 per cent) of the 1,608 cases in the series, the history did not reveal that the patients had been jaundiced at any time.

Symptoms of sepsis with chills and fever were present in 597 (37 per cent) of the cases. These symptoms usually were associated with the attacks of colic and jaundice, but in a few cases recurring chills and fever were the only symptoms present. The chills occasionally were similar to genuine rigor, and were followed by elevation of temperature to 104 or 105 F.

Gastro-intestinal disturbances of one kind or another were reported in most of the cases. Nausea and vomiting occurred in 1,100 (68 per cent), associated with one or more of the attacks. The majority of the

patients complained of chronic dyspepsia, with gas, belching and distress in proportion to the amount of fatty foods and coarse vegetables ingested. This is commonly seen in patients with disease of the gallbladder.

External biliary fistula was present at the time of admission in 39 (2.4 per cent) cases. These occurred in cases in which operation had been performed previously, but in which the obstruction of the common duct had not been relieved.

In the diagnosis of obstructive lesions in the common bile duct, it is important to know whether or not bile is passing from the duct into the duodenum. This can be ascertained easily by passage into the duodenum of a small, soft Rehfuss tube. It has been our experience that when the obstructing lesion is a stone, bile in smaller or larger amounts can be recovered in almost every case, especially if the tube is passed daily for three or four days. This is in contrast to the complete obstructions due to stricture or malignancy of the duct or of the pancreas that sometimes are seen.

Even after a most careful clinical and laboratory study of these cases, the exact diagnosis in a few of them must finally be made on the operating table. This is especially true of the cases of so-called silent stone in the common duct; in these cases, symptoms apparently are absent. The patient with jaundice often presents a difficult problem if one attempts accurately to diagnose the type of lesion which is producing the obstruction, and sometimes the only diagnosis that can be made is of jaundice of the obstructive type. However, if a history is painstakingly obtained, and if the patient is kept for a period of observation in the hospital before operation, surprisingly few mistakes will be made. In the patient who is not jaundiced and in whom the history has been irregular and lacking in one or all of the typical symptoms of stones in the common duct, cholecystography may aid materially in arriving at a diagnosis, especially if the result is positive.

OBSERVATIONS AT OPERATION

In 1,021 (63.5 per cent) of 1,608 cases, stones were found both in the gallbladder and in the common bile duct. In 93 of this group, operations, most of them cholecystostomy, had been performed previously. In 587 (36.5 per cent), stones were found only in the common bile duct. Of the latter group, 149 patients had had the gallbladder removed previously; in the remaining 438, the gallbladder was present but did not contain stones.

We have not attempted to tabulate the number of stones found in the ducts, as in many cases only 1 stone was found, whereas in a few, more than 100 stones were discovered. The common duct that contains

1 stone or more is usually enlarged, and its walls usually are thickened, but sometimes, following cholecystectomy or when the function of the gallbladder has been destroyed by disease, a duct containing no stones may be seen. Frequently when operating, the surgeon is confronted with the problem of whether or not to open the common duct. In many instances, stones cannot be palpated before the duct is opened, especially if they are situated in the lower part of the duct, in the region of the pancreas. It is our practice to explore the duct even when stones cannot be felt, provided that it is unduly enlarged and that there is a definite history of attacks of chills, fever and jaundice. In many instances, on account of a definite clinical history, we have opened the duct and have found stones that could not be palpated before the duct was explored.

The spontaneous formation of a fistula between the gallbladder and an adjacent hollow viscus occurred in 72 patients. In the majority of these, the fistula was between the gallbladder and the duodenum; in a lesser number, the communication was with the colon, and in a few cases, with the stomach.

Pancreatitis was mentioned as an associated lesion in 430 (26 per cent) cases, and marked cholangeitis was seen in 67 (4.2 per cent). Varying degrees of hepatitis and biliary cirrhosis were seen in the liver, especially if the condition was of long standing and if jaundice had occurred frequently.

TECHNIC OF OPERATION

Unfortunately, all of the etiologic factors concerned with the formation of gallstones are not known. Neither is the relationship of infection and metabolic disturbances to the formation of gallstones understood. Often it is difficult to tell whether the primary focus of disease is in the gallbladder, bile ducts or liver, or whether the entire biliary system may even be affected. But in the light of present knowledge, surgical intervention offers the only hope of cure for the patient with gallstones.

The first technical point in the operation is to see to it that the incision is sufficiently large to permit the best possible exposure. Exposure of the operative field is more important in this operation than in almost any other. After the incision has been made and the packing off has been completed, the common bile duct should be freed as completely as possible, so that the different technical steps can be carried out without danger of injury to other structures.

When the duct has been exposed, it is usually best to grasp it with two delicate Allison forceps. In certain cases it will be better to use the stone as a guide, holding the stone with the fingers of one hand and making the incision through the duct, down on the stone. The opening in the duct should be large enough, if dilated, to admit the examining finger. A fairly large longitudinal incision in the duct can readily be repaired without any tendency to the formation of stricture. Not infrequently, especially if the duct is large, a scoop or probe will pass by a

stone, thus giving the impression that no stone is present. However, when the duct is large enough to admit a finger, the likelihood of overlooking a stone is reduced considerably.

After the incision has been made in the duct, the bile, débris and loose stones should be gently sponged out, and then all the other free stones should be removed as gently as possible from the common and hepatic ducts. We are certain that considerable harm can come from irrigation of the bile ducts if too vigorously applied, although several times we have been able to flush stones out of the ducts of the liver that probably could not have been removed in any other way.

Removal of the stone or stones from the ampulla is best accomplished by first passing a scoop into the ampulla, then guiding the scoop, with the fingers outside the duodenum, gradually manipulating the stone until it is crowded into the hollow of the scoop, and holding it in this position as the scoop is gradually withdrawn. We find that the surest way to palpate a small stone in the ampulla, especially when the surrounding pancreatic tissue is swollen, is to pass a probe, as large as will comfortably fit into the common bile duct, gently down into the ampulla, and then to palpate the ampulla, leaving this instrument in place as a guide. In many cases, the duct is greatly elongated, and there may also be considerable enlargement of the head of the pancreas, which makes it difficult to locate the ampulla even when a stone of fair size is present. A large curved hemostat is one of the best instruments for locating the ampulla and also for demonstrating whether or not it is open. We have frequently been able to pass such an instrument into the duodenum when nothing else would go through the ampulla.

We realize how difficult it is to be sure that all stones have been removed. Occasionally some will be overlooked, even when the greatest care has been exercised, and in some instances stones will form again. We do not feel that efforts to clear out all calculi should be carried to the point of too great trauma to the tissues. We have seen one case of stricture following removal of stone from the ampulla. This, apparently, rarely occurs, but severe infection may follow energetic probing and dilating. If the gallbladder has been removed or destroyed, the activity of the sphincter at the ampulla will be overcome, and there will be a free passage for small stones or débris into the duodenum. We believe that it is far more important to provide for prolonged drainage by the insertion of a T-tube, when stone in the common duct occurs, than it is to dilate the passage forcibly into the duodenum. Drainage of the duct should always be carried out after removal of stones, and this is best done with the Deaver T-tube. By this method, complete control of the flow of bile is obtained after the wound has healed around the tube. If the lower end of the duct is opened widely, bile will pass through the tube into the duodenum; whereas if the ampulla is closed because of swelling or another cause, the bile escapes to the outside through the long arm of the tube. When bile is needed for the welfare of the patient, it may often be forced into the duodenum by clamping the outside tube. Another advantage of this plan of

drainage is that this tube may be used as MacArthur suggests, that is, for the administration of fluids, dextrose and any form of liquid nourishment.

It is our practice to remove the gallbladder in all cases of stone of the common duct when jaundice is not present or when the operative risk is not materially increased. When the patient is deeply jaundiced, we feel that the additional operation involved in removal of the gallbladder with exposure of the surface of the liver is not justified, except in an occasional instance. In most of these cases cholecystostomy is done, with removal of the stones, in addition to choledochostomy.

POSTOPERATIVE TREATMENT

The intravenous administration of a 10 per cent solution of dextrose has proved to be a great help in treating patients after operation; this is especially so if the patients are jaundiced or if the liver has been considerably injured by the disease. We give 1 or 2 liters as a routine injection each day for the first few days after operation. As soon as the patient is able to take nourishment, carbohydrates are given freely, and often 30 cc. of karo corn syrup twice daily is prescribed as an aid to recovery of hepatic function.

In the average cases of stone in the common bile duct, the drainage of bile to the outside through the T-tube will begin to diminish after the first week. At the end of the second week considerable bile is usually entering the duodenum, and at this stage we begin to clamp the long arm of the T-tube for a few minutes each day. The time during which the tube is clamped is gradually increased, and usually by the end of the fourth week the tube can be clamped all of the time with perfect comfort to the patient. By this time the stools are well colored with bile, and then the T-tube is removed.

If the patient is deeply jaundiced at the time of the operation, or if marked cholangeitis and hepatitis are present, prolonged drainage is indicated. In such cases, we frequently leave the tube in place for several months, and occasionally for a year.

The most frequent postoperative complications are peritonitis, pneumonia, hemorrhage and hepatic and renal insufficiency. Many patients constitute poor risks from a surgical standpoint on account of age, jaundice and hepatic disease of long standing; it is in this group that most of the deaths occur. In patients who seek relief early in the course of their illness, before their general health has become materially impaired, and before the liver has become extensively diseased, operation can be done with a risk that is very little greater than that encountered in cholecystectomy. In the patient with jaundice, the

tendency to hemorrhage after operation is present, and we feel that small transfusions of whole blood are of definite benefit in controlling the bleeding.

RESULTS

In the series of 1,608 patients, the mortality rate was 6.7 per cent. Various causes were responsible for the number of deaths represented by this percentage, as follows: local or generalized peritonitis, 24 per cent; pneumonia, 24 per cent; hemorrhage in one form or another, 18 per cent; acute or chronic nephritis with renal insufficiency, 10 per cent, and pulmonary embolism, 7 per cent. The remainder of the deaths were due to cardiac failure, suppurative cholangeitis, diabetes mellitus, meningitis, ulcerative colitis and atrophy of the liver with hepatic insufficiency.

The patients who survived the operation were, in the great majority of cases, completely relieved from their symptoms and have remained well. In the follow-up records it is found that 75 (4 per cent) have returned to the clinic because of recurring trouble, and in 55 of these, stones were again removed from the common bile duct.

ANEURYSM OF THE SPLENIC ARTERY

REPORT OF A CASE AND REVIEW OF THE LITERATURE *

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The occurrence of aneurysms of the abdominal vessels is considered unusual, but as the result of improvement in diagnostic technic, aneurysms have come to occupy an important position among the lesions of the abdomen of which there are no pathognomonic signs. Of this group, splenic aneurysms are perhaps the most uncommon, since Anderson and Gray,[1] who recently published an admirable summary of the subject, were able to collect only 58 clinical cases. In but one of these was the lesion diagnosed preoperatively. Schroeder,[2] who made a study of splenic aneurysms, collected statistics from the larger pathologic museums of Europe, and in his series of 32,768 autopsies, only 20 cases of splenic aneurysm are included. Of the clinical cases reported, operation was performed in 15. The diagnosis was made preoperatively only once, by Högler,[3] from the following symptoms and signs: sudden attacks of pain in the upper left quadrant of the abdomen, a filling defect in the stomach along the lesser curvature and a systolic blow over a palpable tumor.

Winckler [4] performed an operation for a splenic aneurysm in which he removed the spleen also. His patient recovered, and lived for twenty-five years. In his paper he considered the advisability of splenectomy in the presence of splenic aneurysm, stating that he felt it to be a hazardous procedure.

Villard and Murard [5] gave an account of a case in which operation was performed for a pancreatic cyst, but an aneurysm of the splenic

* Submitted for publication, Dec. 6, 1930.

* From the Cleveland Clinic.

1. Anderson, W., and Gray, J.: Report of a Case of Aneurysm of the Splenic Artery, with References to 58 Cases Collected by Authors, Brit. J. Surg. **17**:267, 1929.

2. Schroeder, Carl: Ueber einem Fall von Aneurysma der Arteria lienalis, Arch. f. klin. Chir. **132**:175, 1924.

3. Högler, F.: Beitrag zur Klinik des Leber- und Milzarterienaneurysmas, Wien. Arch. f. inn. Med. **1**:543, 1920.

4. Winckler, V.: Ein Fall von Milzexstirpation wegen Aneurysma der Arteria lienalis, Zentralbl. f. Chir. **32**:257, 1905.

5. Villard, E., and Murard, J.: Anévrisme de l'artère splénique, Arch. gén. de chir. **8**:749, 1912.

artery was found. They used a tampon instead of attempting to remove the tumor, and the patient died twelve days later.

In Mulley's [6] case, a diagnosis of left hydronephrosis was made. At operation, a large solid tumor was found near the splenic vessels which, on inspection, proved to be an aneurysm. The spleen was removed along with the tumor, and the patient recovered.

Garland [7] described a case in which rupture of a splenic aneurysm was caused by an abdominal paracentesis, which caused the patient's death.

Smith [8] gave the history of a Negress who was brought into a hospital in shock. A diagnosis of ectopic pregnancy was made. At operation much blood was found in the lesser omental sac, and further examination revealed a splenic aneurysm which had ruptured. The bleeding was controlled with tampons, but the patient died two hours later. In this case the aneurysm had pressed on the pancreas and had caused atrophy.

Lundwall and Gödl [9] described an aneurysm of the splenic artery which ruptured during the ninth month of pregnancy, causing the death of the patient. A supravaginal hysterectomy was done in an attempt to prevent bleeding, the source of which was in the abdominal cavity. Only at autopsy, however, was the lesion of the splenic vessel found.

In Schroeder's [2] case, there was a swelling on the left side, with blood in the stools. At operation he found a cirsoid aneurysm of the splenic artery, with an enlarged spleen weighing 3,000 Gm. The patient died after the operation.

Fitzwilliams [10] performed an exploratory laparotomy for shock combined with abdominal pain. He found a ruptured aneurysm of the splenic artery. The patient died within four hours.

Davis [11] operated because of a tumor which appeared just to the left of the umbilicus. He succeeded in removing the mass, and the patient made an uneventful recovery.

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6. Mulley, K.: Ein Fall von Aneurysma der Arteria lienalis, geheilt durch Splenektomie, Beitr. z. klin. Chir. **111**:205, 1918.

7. Garland, J.: Aneurysm of the Splenic Artery, Rupturing Simultaneously with Paracentesis Abdominis, Boston M. & S. J. **184**:385, 1921.

8. Smith, W. R.: A Case of Ruptured Aneurysm of the Splenic Artery, J. A. M. A. **80**:1692 (June 9) 1923.

9. Lundwall, K., and Gödl, A.: Aneurysm of the Splenic Artery, Arch. f. Gynäk. **118**:177, 1923.

10. Fitzwilliams, D. C. L.: Fatal Case of Aneurysm of the Splenic Artery, Brit. M. J. **2**:803, 1924.

11. Davis, B. F.: Aneurysm of the Splenic Artery: Operative Removal, J. A. M. A. **84**:200 (Jan. 17) 1925.

Näher [12] removed a splenic aneurysm together with the spleen, and his patient was cured.

Saenger [13] gave the history of a patient who suffered from sudden pain in the abdomen followed by collapse. An operation was performed and an eight months' fetus was found. Free blood in the peritoneal cavity led to the discovery of an aneurysm of the splenic vessels.

Goullioud [14] operated in a case in which he found an aneurysm of the splenic artery. He was unable to dissect the mass free, and therefore tied the large vessels entering and leaving it. The patient made an uneventful recovery.

Faehrmann and Ugrümow [15] operated on a man suffering from paroxysmal pain, and found an enlarged spleen with hemorrhagic ascites, together with a bleeding point in the splenic artery. Tampons were used, but the patient died twelve hours later. Autopsy revealed an aneurysm of the splenic vessels.

Marshall [16] performed an operation on a patient who had a wound from a gunshot in the abdomen, and found a pancreatic fistula, which finally closed. Five months later, the patient was readmitted with an aneurysm of the splenic artery. A gauze pack was used to control bleeding, and a pancreatic fistula was again formed.

The following case is presented because of the patient's long illness, the unusual pathologic condition which was found and the favorable outcome of surgical intervention:

REPORT OF CASE

History.—A boy, aged 16 years, was admitted to the Cleveland Clinic on March 15, 1930, complaining of attacks of severe abdominal pain. The mother gave the following history. Shortly after recovery from an attack of whooping cough, which had occurred eight years previously, paroxysms of pain had suddenly developed in the pit of the stomach. These were so intense that the patient would writhe on the floor and apply pressure to his abdomen in an effort to secure relief. The pain was not related to meals, but came on at any time. During the preceding six months, it had occurred more frequently, and at the time of this consultation the patient had as many as two or three attacks a day. Morphine in one-half grain (0.32 mg.) doses afforded some relief. After an attack of pain the stools were tarry, and on examination they were found to contain much blood.

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12. Näher, H.: Aneurysms of Splenic Artery, Deutsche Ztschr. f. Chir. **198**: 118, 1926.

13. Saenger, Hans: Fatal Hemorrhage in Eighth Month of Pregnancy from Rupture of Aneurysm of Splenic Artery, Zentralbl. f. Gynäk. **50**:1324, 1926.

14. Goullioud, M.: Aneurysm of the Splenic Artery with Surgical Ablation, Lyon méd. **142**:353, 1928.

15. Faehrmann, I., and Ugrümow, B.: Aneurysm in Splenic Artery, Arch. f. klin. Chir. **137**:193, 1925.

16. Marshall, C. J.: Traumatic Aneurysm of the Splenic Artery with Rupture and Ligature, Brit. J. Surg. **9**:570, 1922.

The patient had had the usual diseases of childhood. His tonsils were removed when he was 7 years of age, and a biopsy had been done on a gland in the neck in an attempt to rule out Hodgkin's disease. There was no history of respiratory, cardiac or renal trouble. The family history was unimportant.

Examination.—Physical examination revealed a slim, pale, undernourished boy about 50 pounds (22.71 Kg.) underweight for his height. The temperature was 99.4 F., the pulse rate 128 and the blood pressure 100 systolic and 60 diastolic. The skin was a pale yellow, and the mucous membranes were pallid. The head and neck were essentially normal. On examination of the chest, some râles were heard in the upper lobe of the left lung. The heart was normal in size, shape and position, but there was a slight systolic murmur at the apex which was thought to be functional. The abdomen was slightly distended, but no fluid, scars or masses could be detected. The remainder of the physical examination revealed nothing of significance.

Examination of the blood gave the following results: red blood cells, 1,700,000; white blood cells, 4,600, and hemoglobin, 40 per cent. The differential count was: polymorphonuclear cells, 61 per cent; lymphocytes, 39 per cent, and transitional cells, 1 per cent. The red cells showed central pallor and a marked variation in size and shape.

Urinalysis gave negative results.

The chemical analysis of the blood showed the sugar, urea, uric acid, calcium, phosphorus, cholesterol and serum bilirubin to be within normal limits. The Wassermann and Kahn tests of the blood were negative.

Examination of the stool revealed much occult blood but no parasites, and a culture from the stool showed colon bacilli and gram-positive diplococci.

A roentgenogram of the chest indicated that there was considerable fibrosis of the hilus and of the upper lobe of the left lung. A roentgenogram of the abdomen suggested nothing abnormal. A roentgenographic study of the gastro-intestinal tract revealed a functioning gallbladder, a normal stomach, deformity and hypermotility of the duodenum and a smooth and hypermotile colon.

From these observations, a tentatitve diagnosis of chronic pancreatitis was made. Other possibilities considered were diaphragmatic hernia, Meckel's diverticulum and congenital adhesions.

The patient was admitted to the hospital and given a transfusion of 500 cc. of whole blood. He was given a high caloric diet and was placed at rest in bed. The pain continued, and there were no signs of improvement. To ascertain the underlying pathologic process, an exploratory laparotomy was decided on.

Operation and Course.—With the patient under spinal anesthesia, a high left rectus incision was made, extending from the xiphoid process to the umbilicus. No gross pathologic process was found in the stomach. The duodenum apparently was dilated and hypertrophied. No scarring was present in the duodenal wall. Examination of the large bowel disclosed no gross abnormalities. Inspection of the jejunum revealed a tumor just above and to the left of the ligament of Treitz. This tumor was firmly adherent to the intestinal wall and was bound down to the vessels leading to the hilus of the spleen. Palpation showed this mass to be solid and apparently attached to the pancreas. A needle was inserted into the tumor in an effort to ascertain its contents, but nothing could be aspirated. The operator then began to dissect the mass free from the intestine, which proved to be easy. While attempting to liberate the mass from the splenic vessels, hemorrhage occurred, and a transfusion was performed during the operation. Hemostasis was secured with forceps and ligatures. The mass could not be dissected free from the pancreas, and the tail of the pancreas, therefore, was removed with

the tumor. The pancreatic duct was found to be markedly dilated, which in all probability was due to pressure on the pancreas. The operator decided that it would be best to bring the cut end of the pancreatic duct up to the abdominal incision, so that if leakage occurred it would drain to the outside. The abdomen was closed without a drain.

After the operation the patient had a rather high temperature, which gradually subsided and became normal at the end of the sixth day. About the seventh day the pancreatic duct that had been sewed into the abdominal wound showed some tendency to discharge. With cauterization by means of silver nitrate, however, this duct healed satisfactorily.

The patient was seen two months after the operation, and he reported that there had been no recurrence of the pain. He had gained 25 pounds (11.3 Kg.)

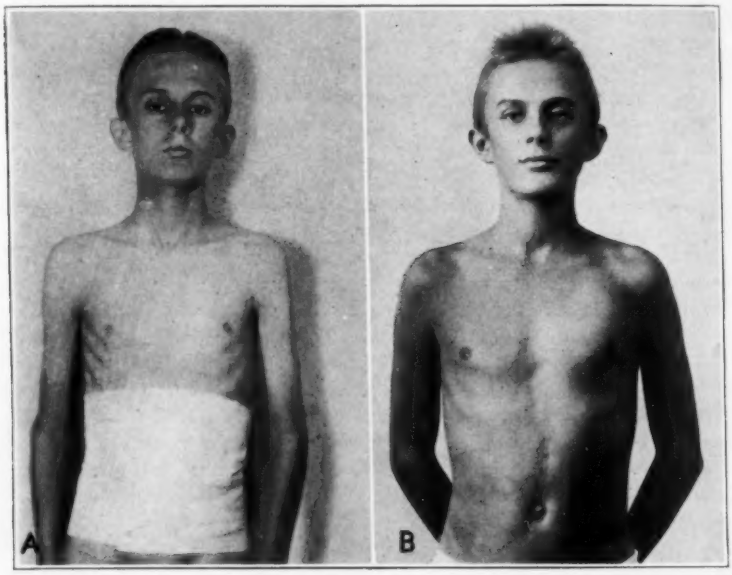

Fig. 1.—*A*, patient two weeks after operation for aneurysm of the splenic artery; *B*, six months after operation. Note the improved state of nutrition.

in weight, and his appetite was much increased. The anemia had progressively lessened until, at the time of this examination, the hemoglobin was 80 per cent and the red cell count 4,500,000.

The patient's gain in weight following operation was slow despite his good appetite. In view of the fact that about a third of the pancreas had been removed, an examination of the feces was made. The stool was very bulky, and contained much undigested material. The normal stool contains from 30,000 to 60,000 units of amylase. (By a unit of amylase is meant the number of cubic centimeters of 1 per cent solution of starch which would be digested by 3,000 cc. of fecal suspension in one-half hour at a temperature of 38 C.) The patient's stool contained less than 3,000 units, and the trypsin content was likewise very low. A fecal suspension of 1.8 cc. failed to digest 5 cc. of a 1 per cent solution of casein.

The stool, stained with sudan III, showed many crystals of fatty acid, and fat globules were present. In order to augment pancreatic digestion, pancreatin,

a dried gland preparation, was given in doses of 10 grains (0.65 Gm.). Following a period of treatment with pancreatin, the patient began to gain weight. While the pancreatin was being administered, the stool was again examined and found to contain the pancreatic enzymes within normal limits. Because of the deficiency in external pancreatic secretion, the blood sugar content and the dextrose tolerance curves were examined, but the patient did not show any evidence of hyperglycemia.

Pathologic Report.—The pathologic report was as follows: The specimen (fig. 2) consisted of a portion of the tail of the pancreas and an attached aneurysmal sac, weighing 40 Gm. The portion of the pancreas, apparently the tail end, measured 5 cm. in length, 2.5 cm. in width and 1 cm. in thickness. It was covered by fibrofatty tissue, and there were numerous lymph nodes in this tissue on the posterior surface of the pancreas. There was a central ductlike structure running longitudinally through the pancreas. This channel was dilated, irregular and surrounded by fibrofatty and pancreatic tissue. Attached to the anterior surface

Fig. 2.—Gross view of specimen of aneurysm of the splenic artery. The threads show the course of the blood vessels through the aneurysm. The vertical thread is passed through the splenic artery, while the horizontal thread runs through a branch of the splenic artery and the aneurysmal sac.

of the pancreas there was a large, round, encapsulated mass which had been ruptured. It consisted of a sac, apparently the wall of a blood vessel, and except for an irregular cavity near the center it was filled with a laminated blood clot. At the posterior extremity there was an opening about 2 mm. in diameter, apparently a blood vessel. Along the superior border and parallel to the pancreas there was a segment of a vein and of an artery, the splenic vessels. From about the middle point of the arterial segment, a branch led into the aneurysmal sac.

On microscopic examination, pancreatic tissue was seen, with extensive fibrosis and loss of glandular tissue. Some of the lobules were represented only by small and by large ducts. There were numerous large masses of islet tissue, which histologically were normal. Neither active acute inflammation nor acute necrosis was seen. Sections from the wall of the aneurysm showed a fibromuscular coat externally and a thick layer of organized and recent blood clot internally.

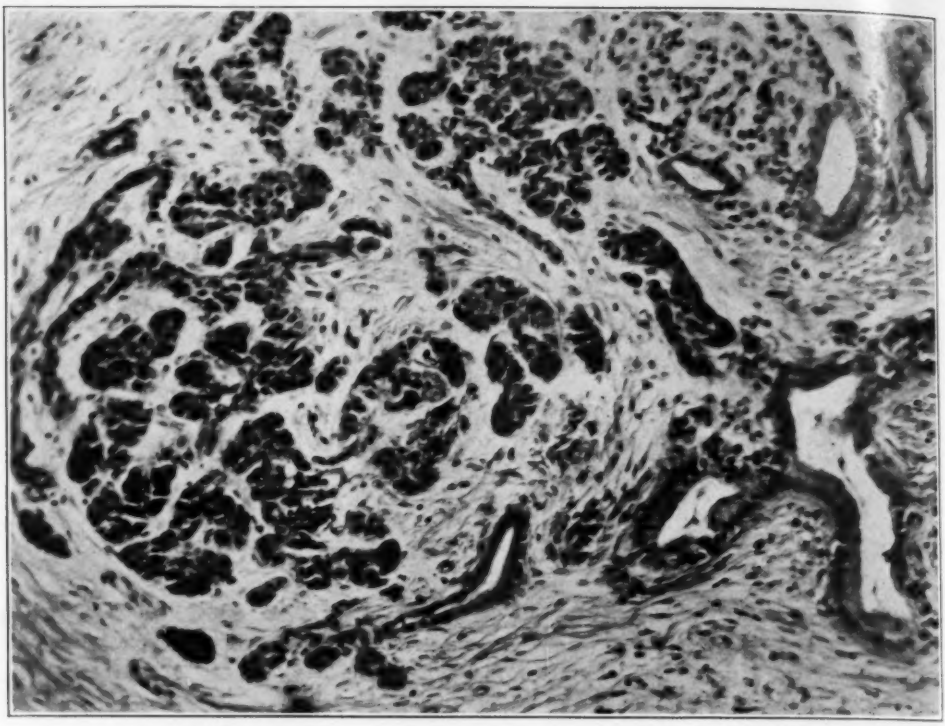

Fig. 3.—Photomicrograph showing atrophy and fibrosis of the pancreatic glandular tissue; × 150.

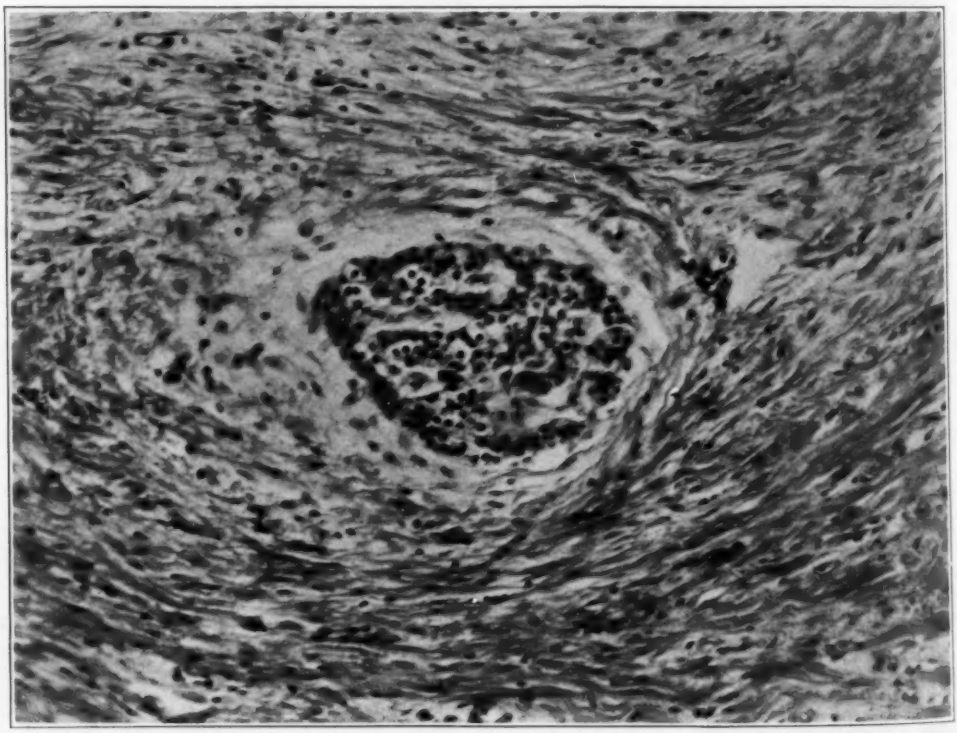

Fig. 4.—Photomicrograph showing complete atrophy of the pancreatic tissue and persistence of the islet tissue; × 150.

COMMENT

The absence of any constant pathognomonic symptom or sign of splenic aneurysm is striking. The two most common observations in cases of aneurysm of the splenic vessels are unheralded paroxysmal attacks of pain in the left side of the epigastrium and tarry stools. The pain is much more severe than that due to organic lesions in the stomach, and should not be mistaken for the pain caused by a gastric ulcer. In addition, there is considerable anemia, and not infrequently there is a pancreatic deficiency which may be detected by examination of the stool for undigested fat. The roentgenologic examination usually does not show anything definite, although in Högler's case,[3] in which the aneurysm was large, the pulsations could be seen under the fluoroscope when a barium meal was given. One feature of the abdominal examination which is usually omitted is auscultation. In only one case was a definite bruit heard over the vessel.

The case report presented here demonstrates that a pancreatic deficiency may accompany a splenic aneurysm. The type of deficiency involves only the glandular tissue concerned with external secretion. The islet tissue remains intact. This observation has been made repeatedly in experimental animals in which the pancreatic duct has been ligated. It is noteworthy that the pancreatin given by mouth corrects the deficiency in pancreatic digestion.

Fifteen cases of splenic aneurysm for which operation has been performed are reported in the literature. In this series, seven patients have recovered from the operation and eight have died, many of the latter having entered the hospital in a state of shock or collapse. In four cases a tampon was used to control bleeding, and in every instance the patient died. In two of the cases in which recovery followed operation, the spleen was removed, and in one, the vessels leaving and entering the aneurysm were tied. In Smith's case [8] the tail of the pancreas was involved, causing atrophy by pressure. In the authors' case also, the tail of the pancreas was involved, with atrophy of the parenchyma and a dilatation of the pancreatic duct.

From a study of the reports of operations performed for splenic aneurysm, it appears that the most important detail is to secure hemostasis, as ligation of the vessels or splenectomy was usually followed by recovery. In all the cases in which a tampon was used to control bleeding, the patients died. The vessels affected can be ligated without serious results. When the splenic artery is involved, ligature of the vessel causes an aseptic atrophy of the spleen, which should cause no mortality, as this has been done many times in experimental animals, and several times in human subjects without any serious effects.

CONCLUSIONS

In cases exhibiting paroxysmal attacks of pain in the upper portion of the abdomen accompanied by gastro-intestinal hemorrhages and an epigastric tumor, and in which roentgenologic examination fails to disclose an organic lesion of the stomach, the possibility of a splenic aneurysm should be considered. In view of the pancreatic involvement in two cases of splenic aneurysm, an examination of the stools for undigested fat should be made in order to determine whether or not a pancreatic deficiency exists. A study of the enzymatic strength of the urine also would be useful, since in diseases of the pancreas an increased amylase content is not infrequently found in the urine. In all cases of abdominal tumor, stethoscopic examination should be made as a routine measure in order to determine the presence or absence of a bruit.

In operating on an aneurysm of the abdominal cavity, accurate hemostasis is essential, as in all cases in which a tampon was used, the patients died. If removal of the spleen is necessary for hemostasis, or ligation of the splenic artery and vein is essential, either may be done without fatal results.

NORMAL THYROID IN RELATION TO THE CLASSIFICATION OF GOITERS

HISTOLOGIC STUDIES *

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After examining patients with thyroid diseases, one is chiefly concerned as to the method of treatment indicated to restore these persons to normal with the shortest period of disability. From writings on both the clinical and the pathologic aspects of thyroid diseases, one is led to believe that there are different types of goiter which remain constant, and that the treatment can be outlined according to the type. Whether goiters of different types do represent definite clinical entities has not been settled, but Hertzler [1] was the first to point out that they may represent merely stages of a continuous disease.

In view of the fact that there is a difference of opinion as to whether one is dealing with a continuous process or different diseases, it was thought advisable to undertake a study of the normal thyroid to determine whether there is a relatively constant histologic picture for the different periods of life from the fetal to the senile stage. In a recent paper [2] a report was made on the study of sections from 107 cases. It was my purpose to obtain sections from a large series of cases in which death was accidental, rather than serial sections from a few cases, as the study of a large group would represent more nearly the pathologic reports on operative specimens. Of 80 cases in which death was accidental the age varied from stillbirth to 89 years. I was unable to find a relatively constant histologic picture for different ages, and the sections were so variable that it was difficult to conclude what was normal. There were also 16 cases in which death resulted from acute diseases and 11 in which it resulted from chronic diseases, but the sections failed to reveal any definite changes.

Figures 1 to 7 inclusive illustrate how variable the histologic changes are in people of apparently normal health. In a specimen

* Submitted for publication, Oct. 20, 1930.
* Read before the Yorkville Medical Society, Oct. 20, 1930.

1. Hertzler, Arthur E.: Pathogenesis of Goiter Considered as One Continuous Disease Process, Arch. Surg. **16**:61 (Jan.) 1928.

2. Hinton, J. William: Histologic Studies of the Thyroid Gland, Am. J. Surg. **11**:269 (Feb.) 1931.

obtained from a female infant, stillborn due to cranial injuries, the epithelial cells were closely spaced with the gland divided into lobules by connective tissue with the absence of acini (fig. 1). In a boy, aged 10 weeks, who died of pneumonia, the acini were well formed with an abundance of both interacinal and interlobular connective tissue (fig. 2). This is contrary to Hertzler's [3] opinion that the connective tissue is more abundant in elderly people. A boy, aged 13 years, who died from

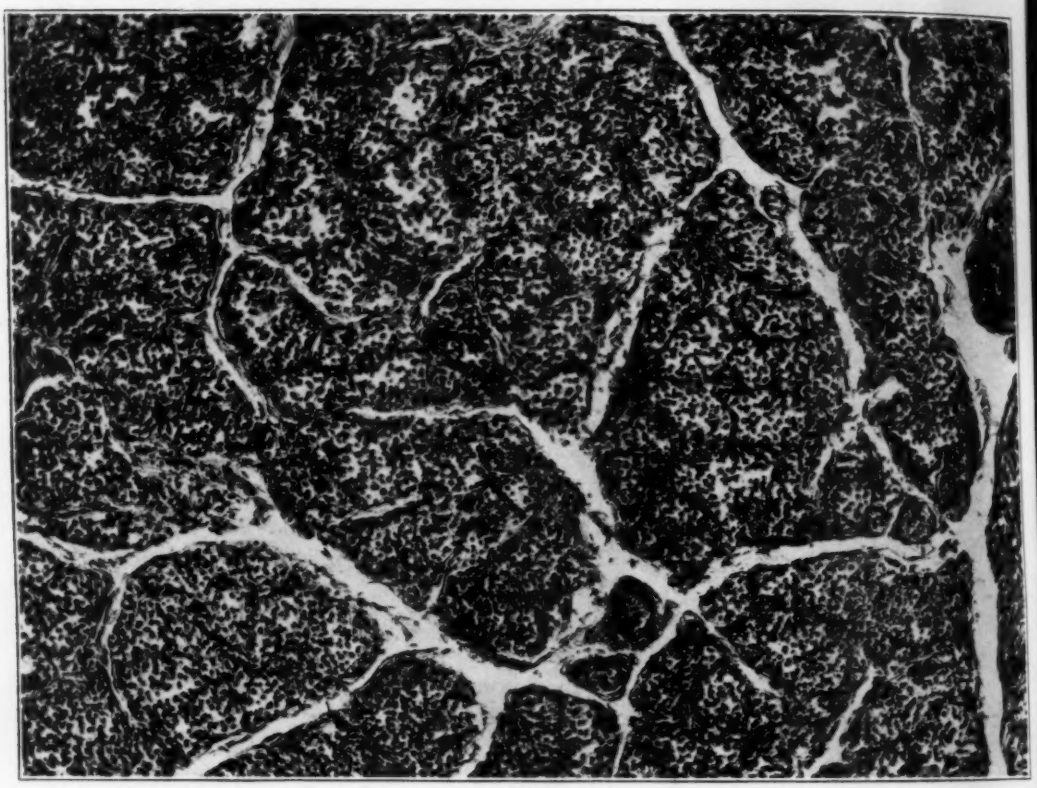

Fig. 1.—Section from a female infant, stillborn, due to cranial injuries.

a fractured skull, showed large acini which contained colloid (fig. 3). In a man, aged 25, who was shot by the police and instantly killed, the acini were very large, contained colloid, and were lined by flat epithelium (fig. 4). In a woman, aged 35, who died from a fractured skull, the gland was divided into lobules by connective tissue but made up chiefly of undifferentiated epithelial cells. A woman, aged 61, committed suicide by strangulation. In the specimen obtained in this case, the

3. Hertzler, Arthur E.: Diseases of the Thyroid Gland, ed. 2, St. Louis, C. V. Mosby Company, 1929.

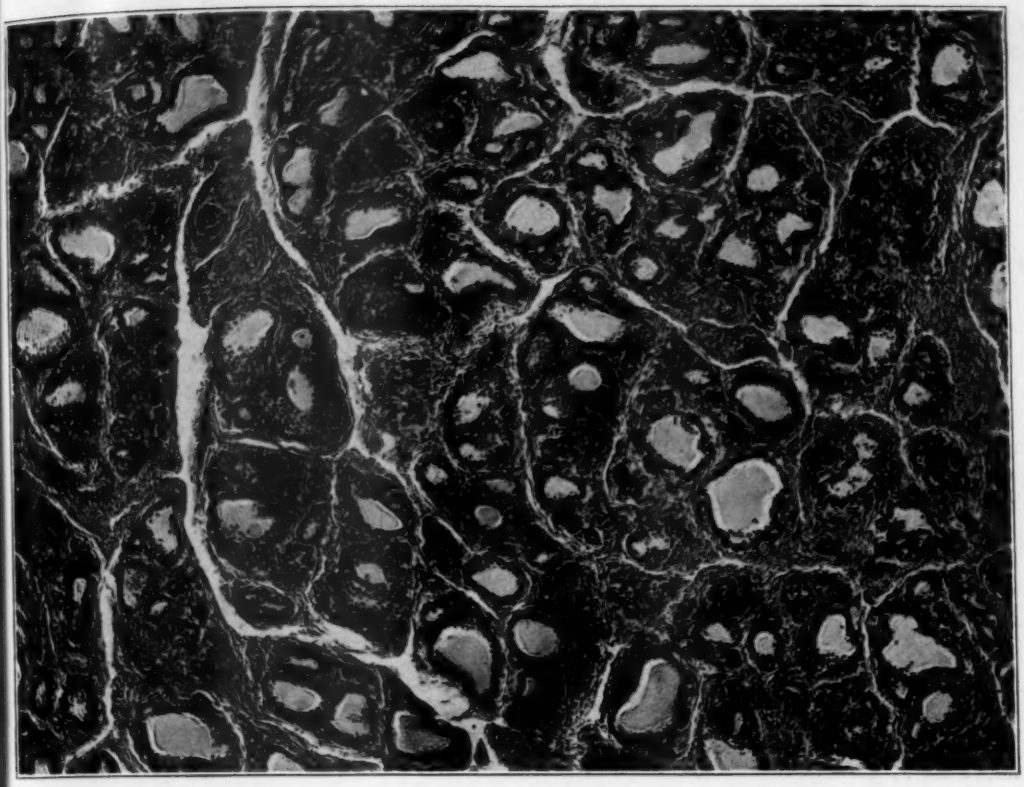

Fig. 2.—Section from a boy, aged 10 weeks, who died of pneumonia.

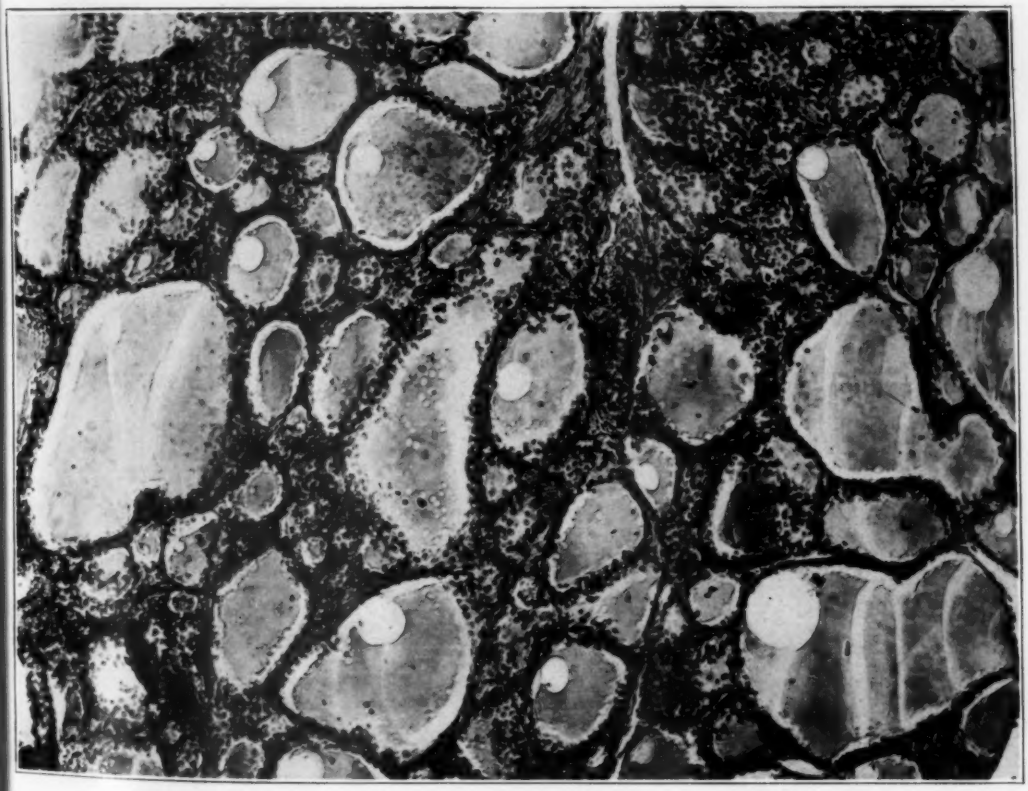

Fig. 3.—Section from a boy, aged 13 years, who died from a fractured skull.

Fig. 4.—Section from a man, aged 25, who was shot by the police and instantly killed.

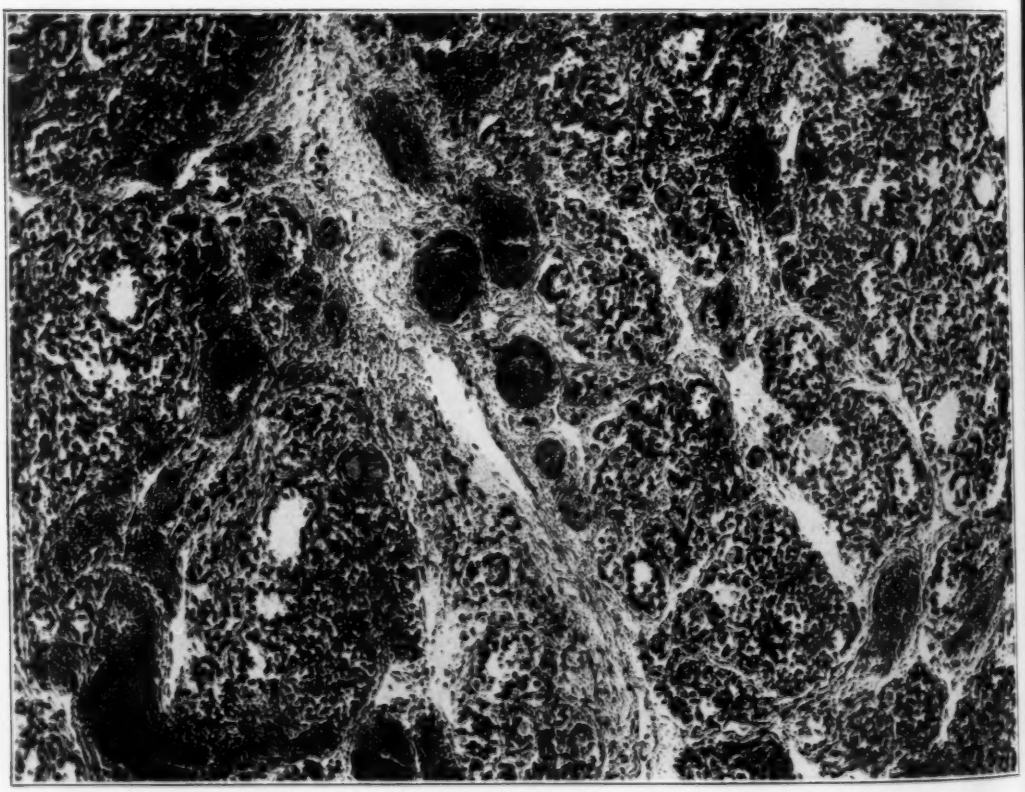

Fig. 5.—Section from a woman, aged 35, who died from fractured skull.

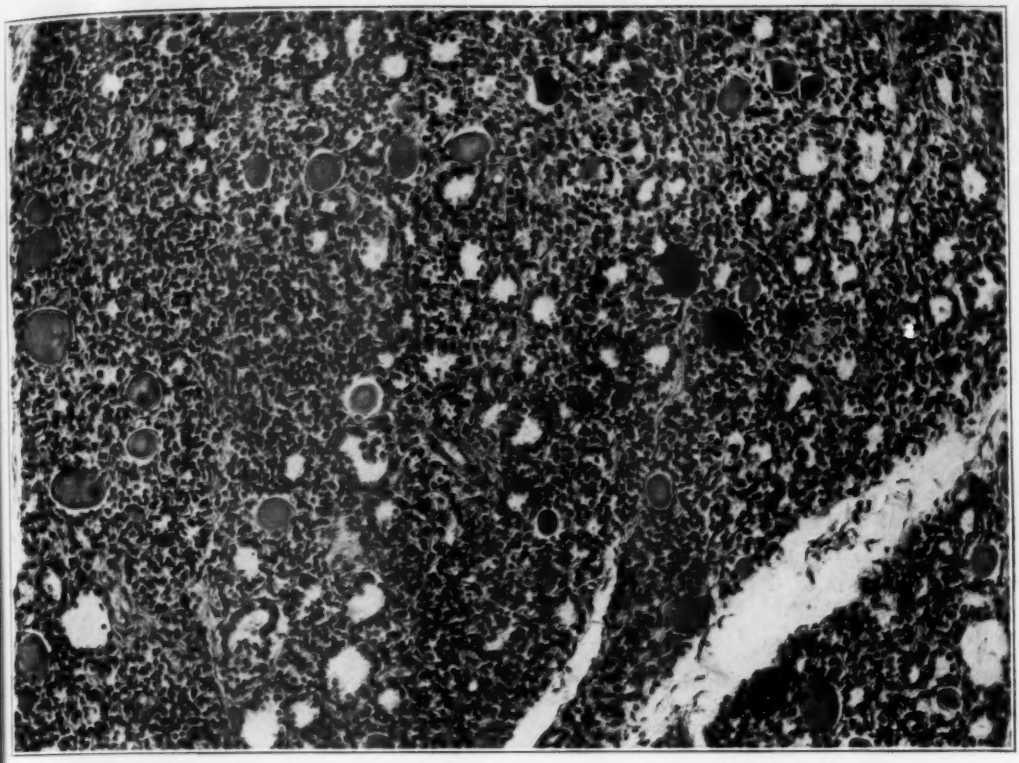

Fig. 6.—Section from a woman, aged 61, who committed suicide by strangulation.

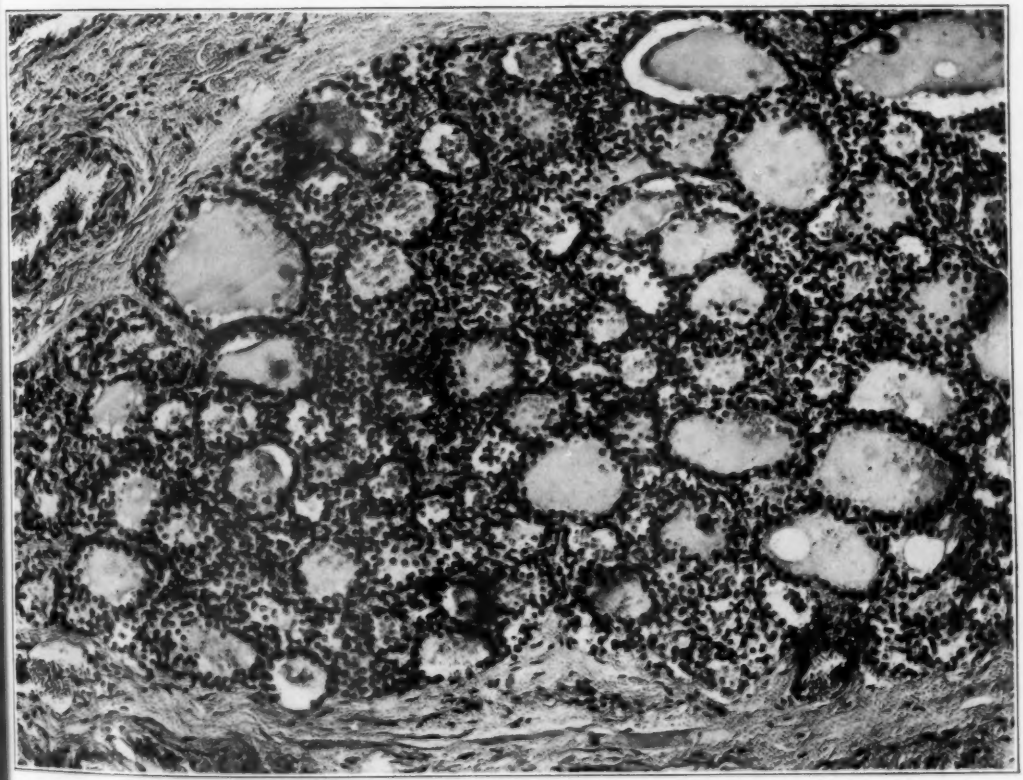

Fig. 7.—Section from a man, aged 75, who died from fractured skull.

acini were small and contained little colloid with scanty interacinal connective tissue (fig. 6). Some well developed acini with other areas of undifferentiated epithelial cells and interlobular connective tissue at the periphery were found in the thyroid of a man, aged 75, who died of a fractured skull (fig. 7).

If the foregoing pathologic changes are so variable, there is little wonder that considerable confusion arises in making an accurate diagnosis in definite goiters. In a previous paper [4] cases were reported in which the clinical diagnosis was of one type of goiter but the pathologic report was of a different type, and if these cases are carefully studied it can be seen that the clinical diagnosis without the knowledge of the pathologic changes was correct; the same holds true for the pathologic diagnosis. The following cases will illustrate the difficulty encountered in making the clinical and pathologic diagnosis coincide.

REPORT OF CASES

Case 1.—A girl, aged 13 years, first seen by me on July 29, 1930, stated that two years previously her mother had noticed a slight swelling of her neck. Her school physician had advised iodide salt, which she used until April, 1930. Not noticing any improvement in her condition, she consulted Dr. Pohlmann of Middletown, N. Y., on April 9, 1930. Her weight was then 117½ pounds (53.3 Kg.), the pulse 82, and there were no symptoms of hyperthyroidism. Dr. Pohlmann's diagnosis was adolescent goiter. Syrup of ferrous iodide, 10 minims (0.6 cc.), three times a day, was prescribed. On June 12 the weight was 107½ pounds (48.7 Kg.), the pulse rate 84, and still there were no symptoms of hyperthyroidism; the iodide was continued. On June 30, the pulse rate was 120, and there was definite evidence of hyperthyroidism. The iodide medication was discontinued; the patient was put to bed and given 30 grains (1.95 Gm.) of triple bromides every four hours. The basal metabolic rate on July 2, was plus 64. On July 15, the patient was slightly improved but mentally confused, and the basal metabolic rate was plus 25. Rest in bed and bromides were continued. On July 22, her mental condition continued the same, the basal metabolic rate being plus 27. An operation was advised, and she entered the Post-Graduate Hospital on July 29, at which time she was 35 pounds (15.9 Kg.) underweight, her best weight being 127 pounds (57.6 Kg.), as against 93 (42.2 Kg.) on entering the hospital. She was irrational, and physical examination revealed a definite exophthalmic goiter. A partial thyroidectomy was done on August 5. Convalescence was uneventful, and the patient was discharged from the hospital on August 14.

The pathologic report was: diffuse parenchymatous exophthalmic goiter (fig. 8). This case was one of typical adolescent goiter which was changed into an exophthalmic goiter by iodine medication.

Case 2.—A nurse, aged 38, was first seen by me on Aug. 4, 1927; she stated that twelve years previously she had been operated on for an adenoma of the isthmus of the thyroid. About one year after this operation she noticed a lump in the right side of her neck. This had increased slightly in size, and about seven weeks before consulting me she had a gastro-intestinal upset from eating sea food. Since

4. Hinton, J. William: The Interchangeable Types of Goiter, Am.J.Surg. **7**: 313 (Sept.) 1929.

that time she had lost 20 pounds (9 Kg.) in weight, and had palpitation of the heart and shortness of breath on going up stairs. Otherwise she felt well. Her menstrual periods had been scanty during the last few months. Examination revealed no evidence of exophthalmos in the right eye. The left eye had been enucleated following an accident at the age of 2 years. At the time of examination there was a nodular mass involving the right lobe without a thrill, and the pulse rate was 108. A diagnosis of adenoma of the thyroid with hyperthyroidism was made. On August 4, the basal metabolic rate was plus 45. The patient

Fig. 8.—Infolding of epithelium in alveoli and little colloid.

was advised to enter the hospital for operation, which she did, and was operated on on August 22. She made an uneventful recovery, being discharged from the hospital on August 30.

The pathologic report was hyperplastic exophthalmic goiter in a stage of remission at the time (fig. 9). This case was considered one of typical adenomatous goiter with hyperthyroidism, and an exophthalmic goiter was not suspected until the pathologic report was received.

Case 3.—A woman, aged 26, was first seen by me on Nov. 30, 1927, complaining of a swelling in her neck which she had had for one year. Friends first noticed a lump in the right side of her neck, but at that time she had no symptoms refer-

able to goiter. Occasionally sensations of pressure and choking were noticed, but otherwise she felt well. Examination gave negative results, with the exception of a definite mass involving the right lobe of the thyroid. The left lobe was normal. Her weight was 133¾ pounds (60.4 Kg.), and her pulse rate 100. Diagnosis of adenoma of the thyroid was made. On Dec. 2, 1927, the basal metabolic rate was plus 3. The patient was informed that she had the type of goiter that could not be treated by medication, but as I had treated her sister for a colloid goiter with a satisfactory result, she demanded medication before submitting to an operation;

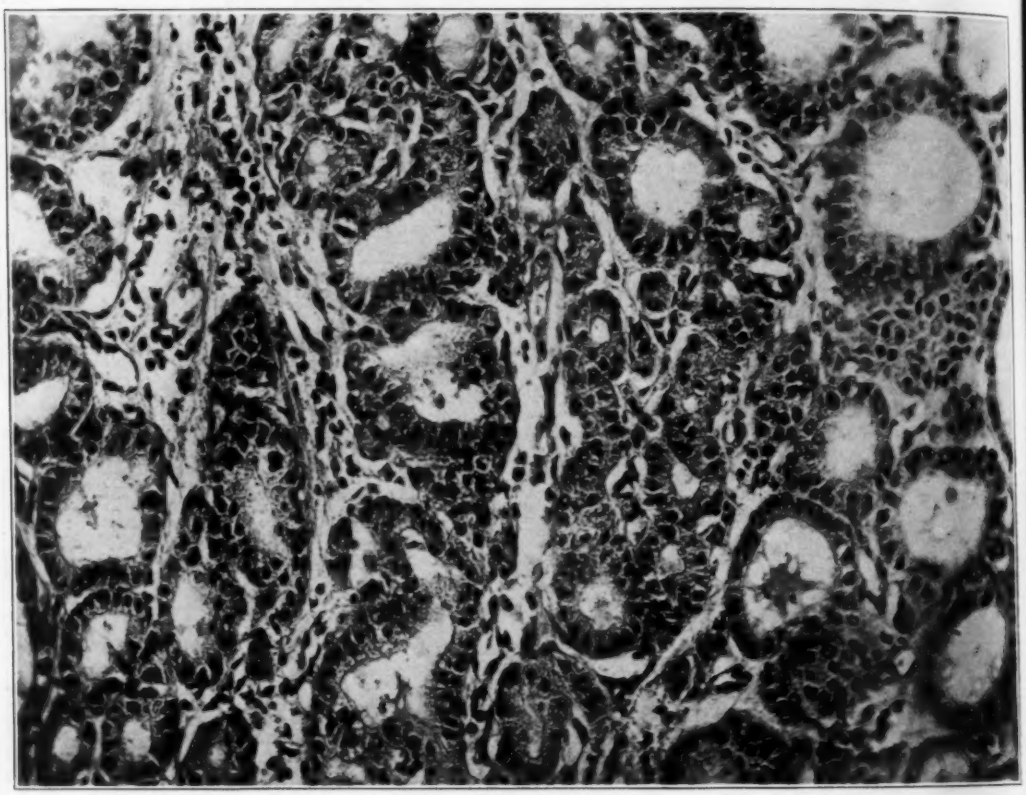

Fig. 9.—Diffuse epithelial hyperplasia with high columnar epithelium, narrow lumen with infolding and with little colloid; active stage.

hence she was given thyroid extract, 1 grain (0.065 Gm.) three times daily. She was next seen on Jan. 18, 1928, at which time her weight was 137¼ pounds (62.2 Kg.) and her pulse rate 90. She had no complaints, but the condition of her neck remained unchanged. She was given thyroid extract, one-half grain (0.32 mg.), three times daily. On March 21, she returned stating she had nausea and vomiting, had been bothered with diarrhea for two weeks and was beginning to feel ill. She complained of nervousness and palpitation, and was losing weight. Examination revealed an enlargement over the region of the thyroid with a definite thrill over it, and a beginning exophthalmos. Diagnosis was then made of

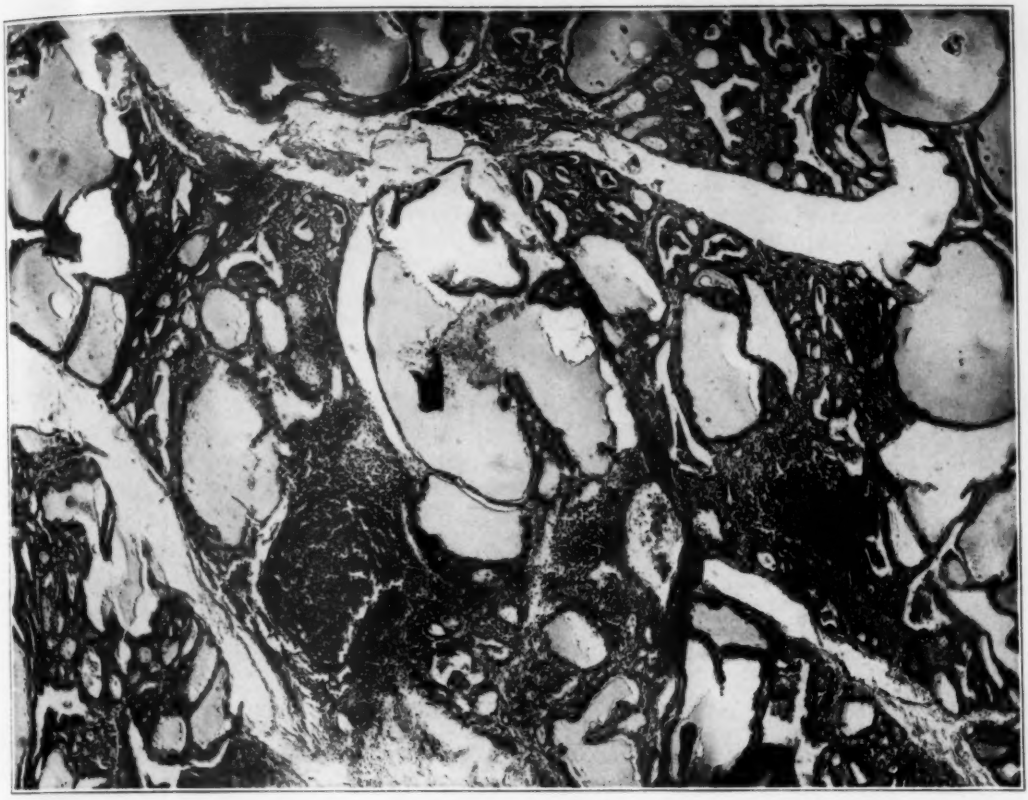

Fig. 10.—Diffuse epithelial hyperplasia. Some areas show narrow alveoli with little colloid and high epithelial lining, others contain much colloid; numerous lymph follicles are seen in the stroma.

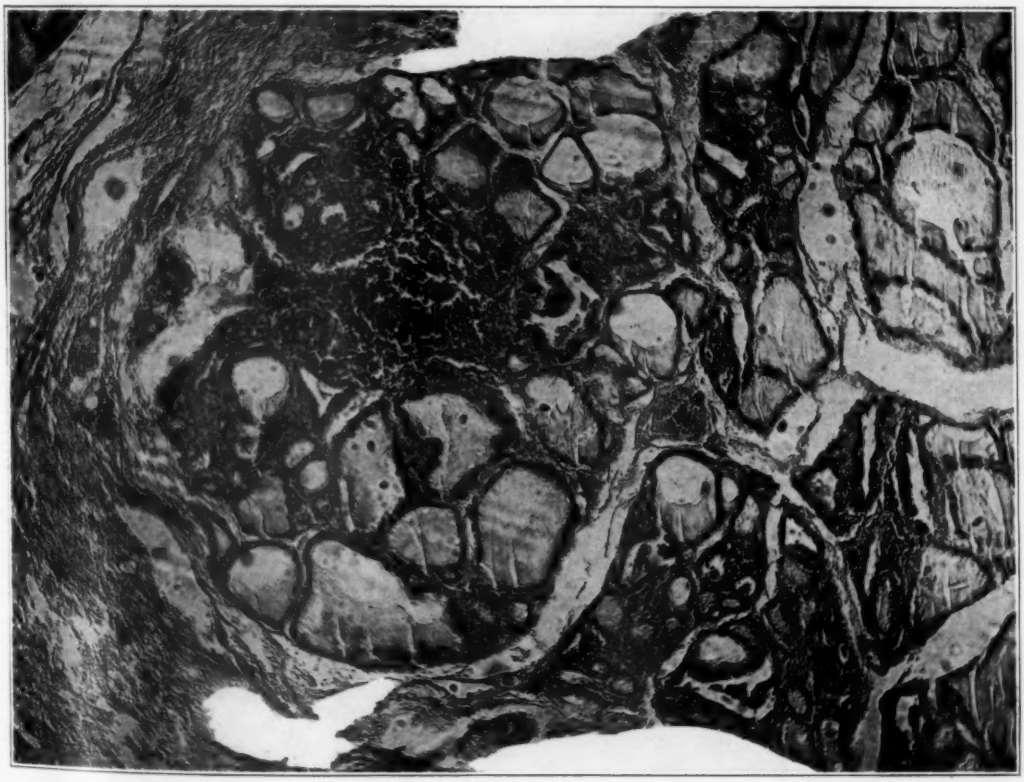

Fig. 11.—Diffuse epithelial hyperplasia with infolding, in some areas more marked than in others. Lymph follicles are seen in the stroma.

exophthalmic goiter. The patient was advised to enter the hospital for observation and operation, which she did on March 22, 1928. On March 26, the basal metabolic rate was plus 60. The weight was 105 pounds (47.6 Kg.) and the pulse rate was 160. The patient was operated on on April 2, and made an uneventful recovery.

The pathologic report was exophthalmic goiter in the stage of remission (fig. 10). From the course of this case one can see a nodular type of goiter changed clinically to an exophthalmic goiter by thyroid medication.

CASE 4.—A woman, aged 33, stated that in September, 1927, she consulted her physician for a swelling of her left ankle and a goiter. At that time she was found to have a phlebitis of the left ankle. On communicating with her physician, Dr. Felder, I found the patient had a colloid enlargement of her thyroid, without symptoms. She was not given any thyroid or iodine medication, but five months later, as her mother had died from an exophthalmic goiter, she consulted a thyroid specialist in New York, for she was rather conscious of the slight fulness in her neck. There were no symptoms referable to the thyroid at that time. On February 4, 1928, the basal metabolic rate was minus 1. The patient was informed that she had no thyroid disturbance, but was given a compound solution of iodine, 3 minims (0.18 cc.) three times a day. Three months later she had lost 8 or 10 pounds (3.6 or 4.5 Kg.) in weight, her eyes were enlarged and she was nervous and quite irritable, and bothered with palpitation. She consulted another physician who told her she had exophthalmic goiter. She was given 1 grain of mercuric iodide once a day and advised to have roentgen therapy. She received several treatments and showed improvement, but four months later, as she was not feeling entirely well, she consulted Dr. Carter, at which time her weight was 118 pounds (53.5 Kg.), as against her best weight of 135 pounds (61.2 Kg.). On October 27, the basal metabolic rate was 3 below the average normal. I saw this patient in consultation with Dr. Carter on October 28, at which time there was definite evidence of enlargement of the thyroid with a thrill over it, and it was quite apparent that the patient was suffering from an exophthalmic goiter. Thyroidectomy was performed on November 5, by Dr. Carter.

The pathologic diagnosis was exophthalmic goiter in the resting stage (fig. 11). In this case one sees a colloid goiter which was changed to the exophthalmic type by the administration of iodine.

COMMENT

When the normal picture is so variable and the clinical and pathologic pictures of different types of goiter are interchangeable, it makes one wonder if the past conception of the different types as clinical entities was not wrong and the types merely represented stages of a continuous disease, as maintained by Hertzler. If so, the treatment of goiters might be simplified, and instead of there being medical treatment for one type and surgical treatment for another, the patient should first be treated medically, if after careful physical examination and metabolic studies there is no evidence of an encapsulated tumor, hyperthyroidism or symptoms of pressure which constitute definite indications for surgical intervention.

125 East Seventy-Second Street.

HEPATOGENOUS CHOLECYSTITIS *

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AND
LEO HRDINA
CHICAGO

The route of infection to the gallbladder has been studied by many observers, and three possible sources of infection have long been recognized as likely. The well known fact that the blood in bacteremia passes many organisms into the bile has been used by many observers as an argument in favor of the biliary origin of cholecystitis. Others are inclined to favor the hematogenous theory, largely on account of the experiments of Rosenow [1] on the elective localization of certain strains of streptococci. More recently, the studies of Graham [2] and his co-workers on the absorption of dyes or particulate matter from the region of the gallbladder has brought into prominence the possibility of a carrying of bacteria in the lymph to the gallbladder from the adjacent viscera, especially the liver.

Recent studies on the bacterial flora of the normal liver have again suggested the importance of the latter route of infection, i. e., by direct extension from the liver. In 1909, Wolbach and Saiki [3] described an anaerobic spore-forming bacillus as a common inhabitant of livers of normal dogs. In 1927, Berg, Zaw and Jobling [4] confirmed these observations, although they found the bile uniformly sterile. More recently, Ellis and Dragstedt [5] have shown that the death from autolysis of the liver in vivo was due to infection of the implanted material with this bacillus, and that sterile implanted liver did not produce any toxemia in its autolysis. Rewbridge [6] showed that the so-called biliary

* Submitted for publication, Nov. 21, 1930.

* From the Department of Surgery, the University of Chicago.

1. Rosenow, E. C.: Focal Infection and the Localization of Bacteria, Surg. Gynec. Obst. **33**:19, 1921.

2. Graham: Inflammation Accompanied by Cholecystitis, Surg Gynec. Obst. **26**:521, 1918.

3. Wolbach, S. B., and Saiki, Tadasee: A New Anaerobic Spore-Bearing Bacterium Commonly Present in the Liver of Healthy Dogs, J. M. Research **21**: 267, 1909.

4. Berg, B. N.; Zaw, Z. D., and Jobling, J. W.: Bactericidal Function of Liver, Proc. Soc. Exper. Biol. & Med. **21**:433, 1927.

5. Ellis, J. C., and Dragstedt, L. R.: Liver Autolysis in Vivo, Arch. Surg. **20**:8 (Jan.) 1930.

6. Rewbridge, A. G.: Etiological Rôle of Bacteria in Bile Peritonitis, Proc. Soc. Exper. Biol. & Med. **27**:528, 1930.

peritonitis was due to this organism, and that intraperitoneal injection of sterile bile or even of sterile pure bile salts was capable of producing an infection by this organism. We [7] also showed that implantation into the abdomen of normal animals of sterile liver or liver extract, if the material was finely divided, would provoke such an infection. Careful bacteriologic studies of this organism in our laboratory have shown that it is without a doubt the Welch bacillus (published elsewhere). It has been found in over 200 experiments in both dogs and other animals. Finally, we wish to refer to the experiments of Arnold [8] in which he showed that under quite physiologic conditions of digestion there is a passage of bacteria through the intestinal wall so free that they may be found in the lymph of the thoracic duct in numbers as high as 1,000 per cubic millimeter. With this enormous seeding of the tissues with bacteria, which must occur daily, one assumes that it is but natural that the spore-bearers should be more resistant to destruction and that they should be the predominant element in the flora. The comparative richness of the flora of the liver is, of course, due to the fact that bacteria, being particulate matter, are taken up by the reticulo-endothelial system, which is so largely localized there.

In the preparation of jaundiced dogs for some experimental studies on jaundice, it was observed that the mortality rate was high and out of proportion to the severity of the operation, and that in some cases frank cholecystitis had developed. This was especially noted in those dogs that had had the cystic duct ligated and the gallbladder emptied, as recommended by Rous and McMaster [9] in their preparation for biliary fistulas. Empyema of the gallbladder in one case and culture of *B. welchii* from another prompted the following series of experiments.

EXPERIMENTAL WORK

With these points in view, a series of twenty-five dogs were studied in which biliary stasis had been produced. Twelve dogs had a simple ligation of the cystic duct. In this series extreme care was used to avoid the cystic artery. This is much easier in dogs than in man, as the artery joins the gallbladder at a greater distance from the common duct. In five dogs the common duct was ligated near the duodenum and in six both the common and the cystic duct were ligated. In two, the common duct was ligated, and, in addition, bilateral nephrectomy was performed in order to increase the intensity of the jaundice.

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7. Andrews, E., and Hrdina, L.: Liver Autolysis in Vivo, Proc. Soc. Exper. Biol. & Med. **27**:987, 1930.

8. Arnold, L.: Alterations in the Endogenous Enteric Bacterial Flora and Microbic Permeability of the Intestinal Wall, J. Hyg. **29**:82, 1929.

9. Rous, P., and McMaster, P. D.: Sterile Drainage of Intraabdominal Ducts as Applied to the Common Duct, J. Exper. Med. **37**:11, 1923.

These dogs were killed at various intervals from twenty-four hours to two months, the bile cultivated, and histologic examinations of the gallbladder made. The dogs were all killed by electrocution, and the cultures were made at once in order to rule out any possibility of postmortem contamination. In many cases sections of the liver were made as well, and in one series the gallbladder and adjacent liver fixed en masse so as to get continuous sections of the two.

RESULTS

The results of the cultures are shown in the table. As a control for this work, the reader is referred to the paper by Rewbridge,[6] who

Cultures of Bile in Dogs

Dog	Operation	Duration of Experiment	Culture
	Dogs With Biliary Stasis		
8	Ligation of cystic duct	17 days	B. welchii
11	Ligation of cystic duct	1 month	Diplococci
14	Ligation of cystic duct	3 days	B. welchii and streptococci
16	Ligation of cystic duct	3 days	B. welchii, streptococci and staphylococci
17	Ligation of cystic duct	3 days	B. coli
20	Ligation of cystic duct	3 days	Staphylococci
26	Ligation of cystic duct	3 days	B. welchii
942	Ligation of cystic duct	57 days	Diplococci
949	Ligation of cystic duct	6 days	Sterile
953	Ligation of cystic duct	57 days	Sterile
144	Ligation of common duct	3 days	Staphylococci
145	Ligation of common duct	3 days	Diplococci
146	Ligation of common duct	3 days	Diplococci
147	Ligation of common duct	3 days	Staphylococci
149	Ligation of common duct	3 days	Diplococci
802	Ligation of common and cystic ducts	4 days	B. welchii
803	Ligation of common and cystic ducts	20 days	B. welchii and diplococci
820	Ligation of common and cystic ducts	8 days	B. welchii
831	Ligation of common and cystic ducts	8 days	B. welchii
834	Ligation of common and cystic ducts	3 days	B. welchii
836	Ligation of common and cystic ducts	12 days	Diplococci
	Dogs With No Pathologic Process		
935	Ligation of cystic duct	Culture taken 24 hours after operation	B. welchii
956	Ligation of cystic duct	Culture taken 24 hours after operation	Sterile
937	Ligation of common duct and bilateral nephrectomy	3 days	B. welchii
954	Ligation of common duct and bilateral nephrectomy	3 days	B. welchii

showed that in our laboratory at least the bile of normal dogs is uniformly sterile. This agrees with the observations of most other investigators, although exceptions have been noted. It depends, one may assume, on the conditions under which the dogs are kept as well as on the technic of making the cultures. In the normal dog, the wall of the gallbladder is often found infected or at least containing organisms, but the bile is usually sterile.

The results of the cultures in the different series may be summarized as follows:

1. In the series in which the cystic duct was ligated, seven of the twelve dogs showed *B. welchii*, five cocci and colon bacilli and only two were sterile.

2. In the series in which the common duct was ligated all showed cocci, and in the two in which double nephrectomy was added, *B. welchii.*

3. In the series in which both ducts were ligated, five of the six showed *B. welchii* and three cocci, all having some infection.

It is evident, therefore, that the presence of biliary stasis favors the prompt infection of the bile and that the predominant flora is that of the liver, the anaerobic type.

The pathologic changes in these experiments are of great interest, as they revealed the fact that the resulting inflammation of the gallbladder which occurred in about two thirds of the cases was undoubtedly of hepatic origin. In the early stages of the cholecystitis in a number

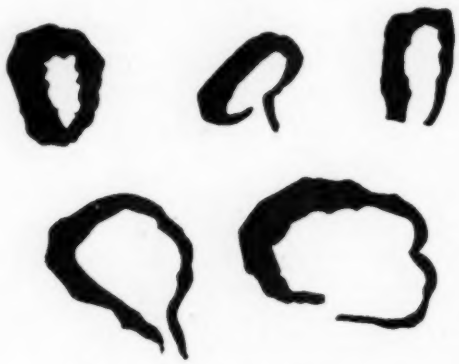

Fig. 1.—Series of sections through fixed gallbladders showing unilateral thickening of the walls. This discrepancy is even more marked in the fresh tissue. Hepatic surfaces are seen to the left.

of the cases the inflammation was confined to the hepatic surface of the viscus while the peritoneal or free side was quite normal. In the later stages this infection extended all the way around the gallbladder. Some of such unilaterally inflamed gallbladders are shown in figure 1. These are all taken from material which has been run through fixatives so that considerable contraction has taken place and the disproportion between the two sides is not as marked as in the fresh specimens. It is quite apparent, however, that the hepatic surfaces are very much more thickened than the free surfaces. Figure 2 is a photograph of a fresh specimen in which the unilateral nature of the process is still more obvious. This phenomenon is much more marked in cases in which the cystic duct has been ligated, but following ligation of the common duct it can be seen to a lesser degree grossly and is quite evident microscopically. In the cases in which the common duct has

been ligated its onset is also more delayed, while in obstruction of the cystic duct it begins at once and can best be demonstrated about the third day, although changes can be seen in twenty-four hours.

Figure 3 illustrates the appearance under very low power magnification of such a specimen. The hepatic surface can be seen to be about three times as thick as the free side. The inflammation involves the outer coats for the most part. The muscularis is thickened to a much lesser extent, and the mucosa is nearly normal. On the peritoneal side the mucosa is normal, as is the muscular coat, but there is a slight thickening of the serous layer.

In all cases it is evident that the mucosa is the last of the coats to be involved. Figure 4 shows the mucosa under higher power magnification; it is quite free from infiltration, although in the same

Fig. 2.—Photograph of a fresh specimen showing thickening of the hepatic surface but not of the peritoneal surface. Note the gelatinous edema of the space between the gallbladder and the liver.

gallbladder the edge of the liver and tissues between the liver and gallbladder were edematous and infiltrated with leukocytes. Even in the later stages the outer layers of epithelial cells tend to remain normal while there is a collection of round cells and fewer polymorphonuclears in the submucous follicles (fig. 5). This condition is never extensive, and only a few such follicles were found in our entire series; they are occasionally to be seen in the gallbladders of normal dogs, although not quite so extensively as in the one here pictured.

The earliest lesions to be found are in the margins of the liver adjacent to the gallbladder and in the space between the gallbladder and the liver. This space often becomes exceedingly edematous, and even grossly can be seen as a gelatinous layer 0.5 cm. thick. In this space bacteria were seen in many of our preparations. Cellular infiltration of this tissue soon follows, as illustrated in figure 6. This may

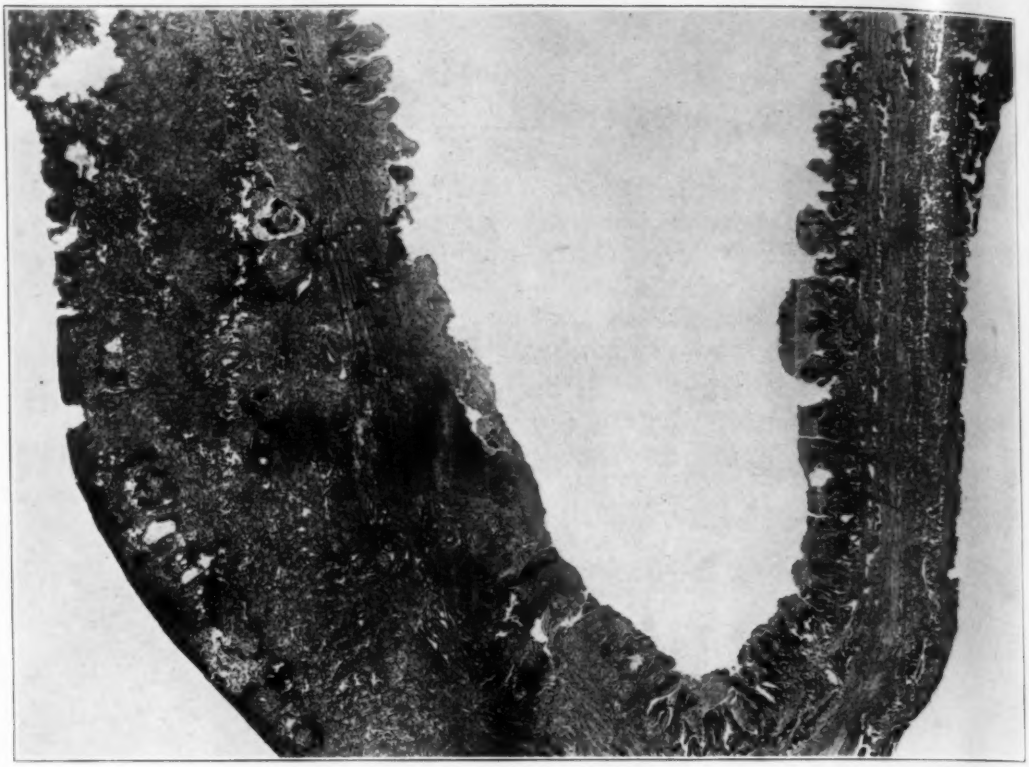

Fig. 3.—Hepatic surface below. Note the unilateral thickening of the outer coats of the gall-bladder and the comparative freedom of the mucosa three days after ligation of the cystic duct. Reduced from a magnification of × 17.

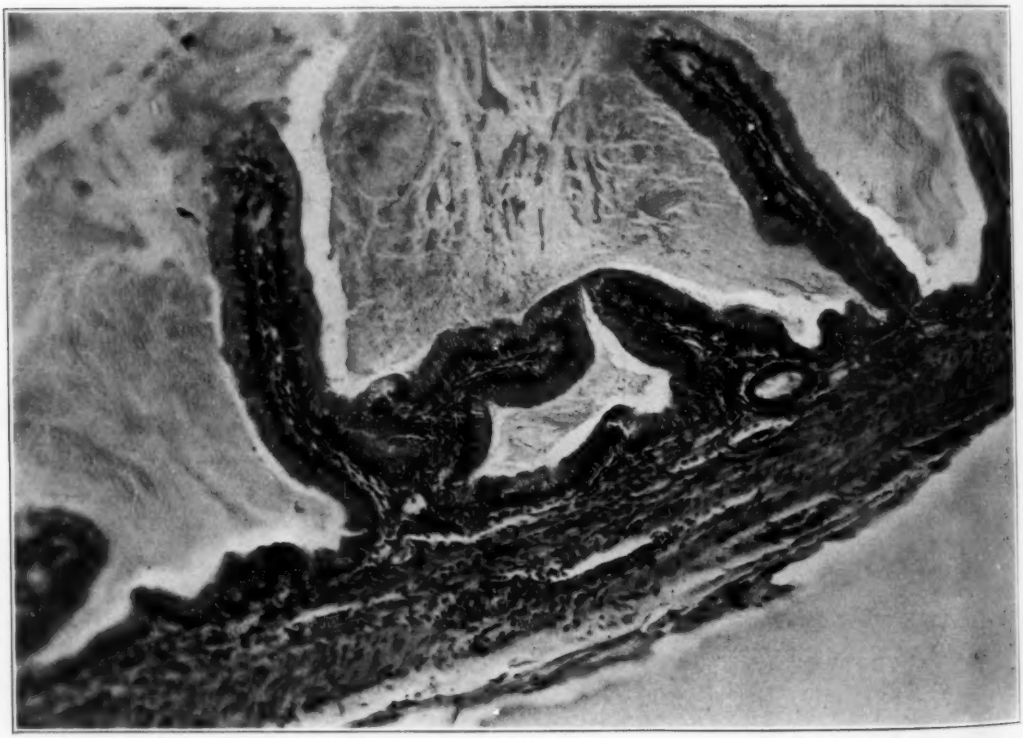

Fig. 4.—Normal mucosa six days after ligation of the cystic duct. There was marked infection of the other layers. See figure 6. Reduced from a magnification of × 130.

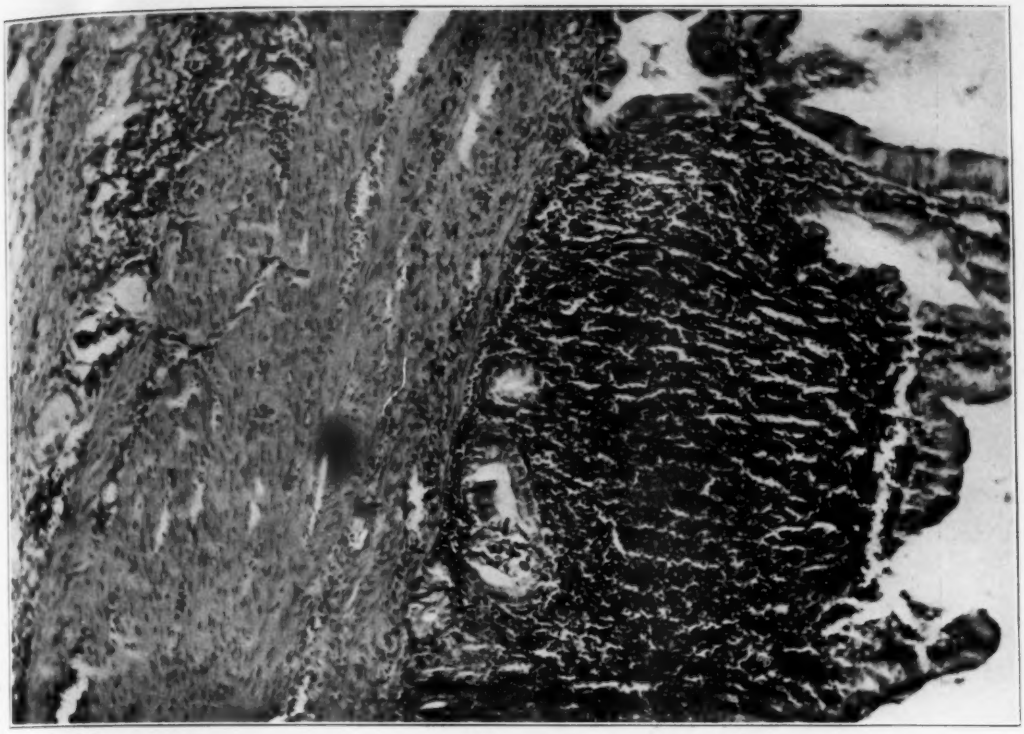

Fig. 5.—Later stage fifty-seven days after operation. A follicle is seen in the submucosa. Reduced from a magnification of × 130.

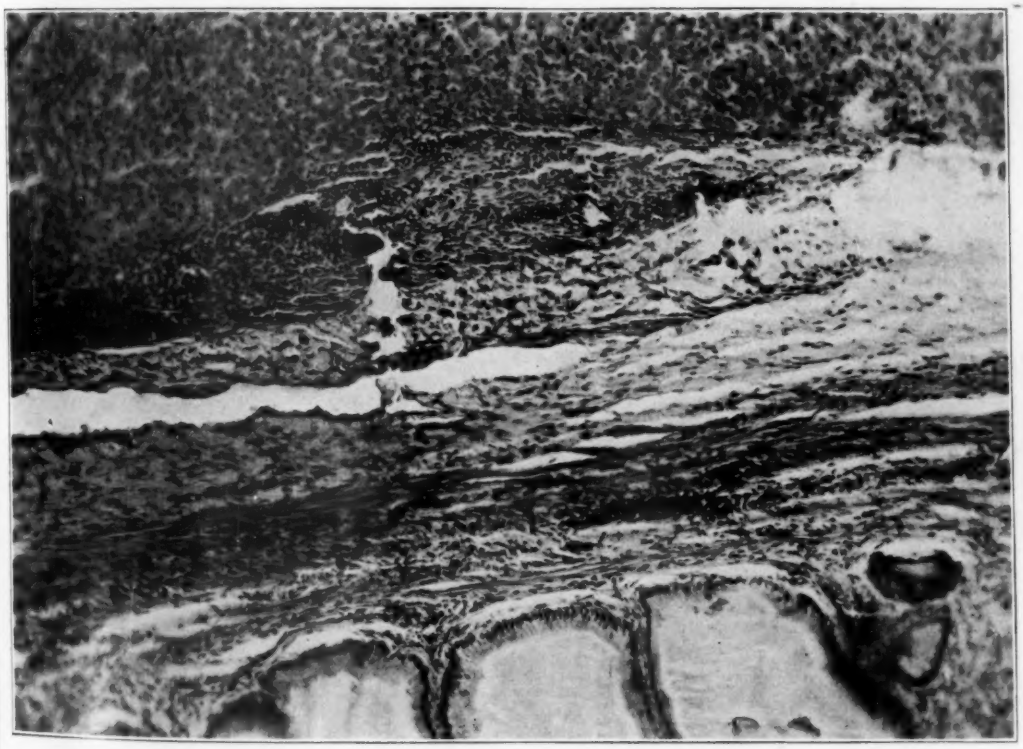

Fig. 6.—Same as figure 4 showing dense infiltration of hepatic tissue adjacent to the gallbladder and slight infiltration of the tissue between the liver and the gallbladder. Note the normal mucosa. Reduced from a magnification of × 130.

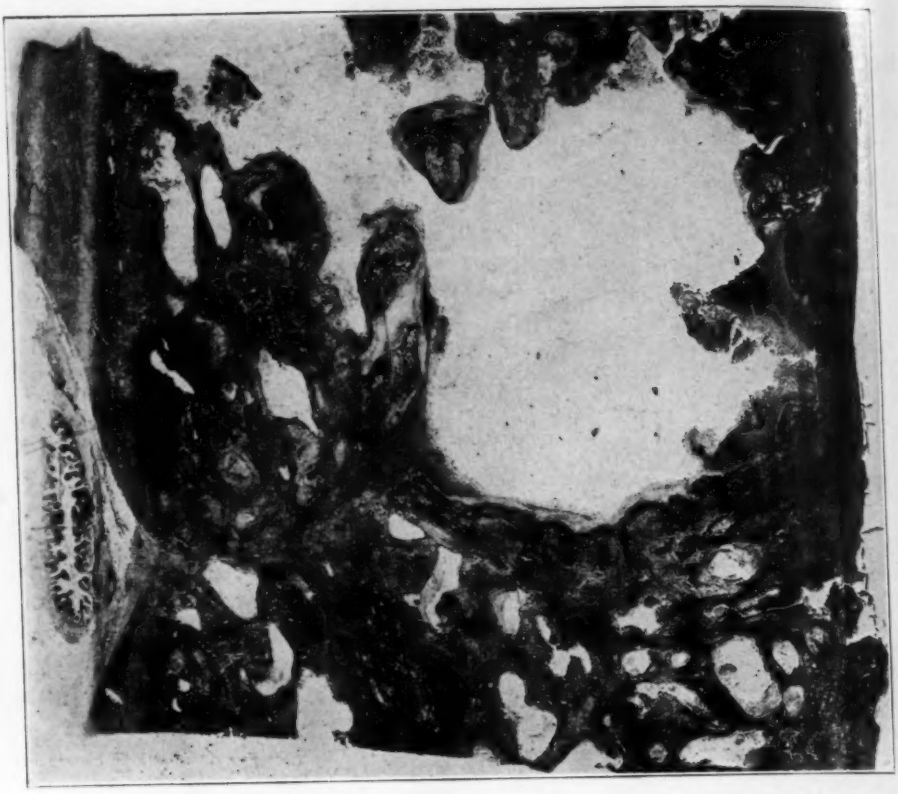

Fig. 7.—The hole in the center is the gallbladder. Note how the hepatic tissue is riddled with gas bubbles; × 4.

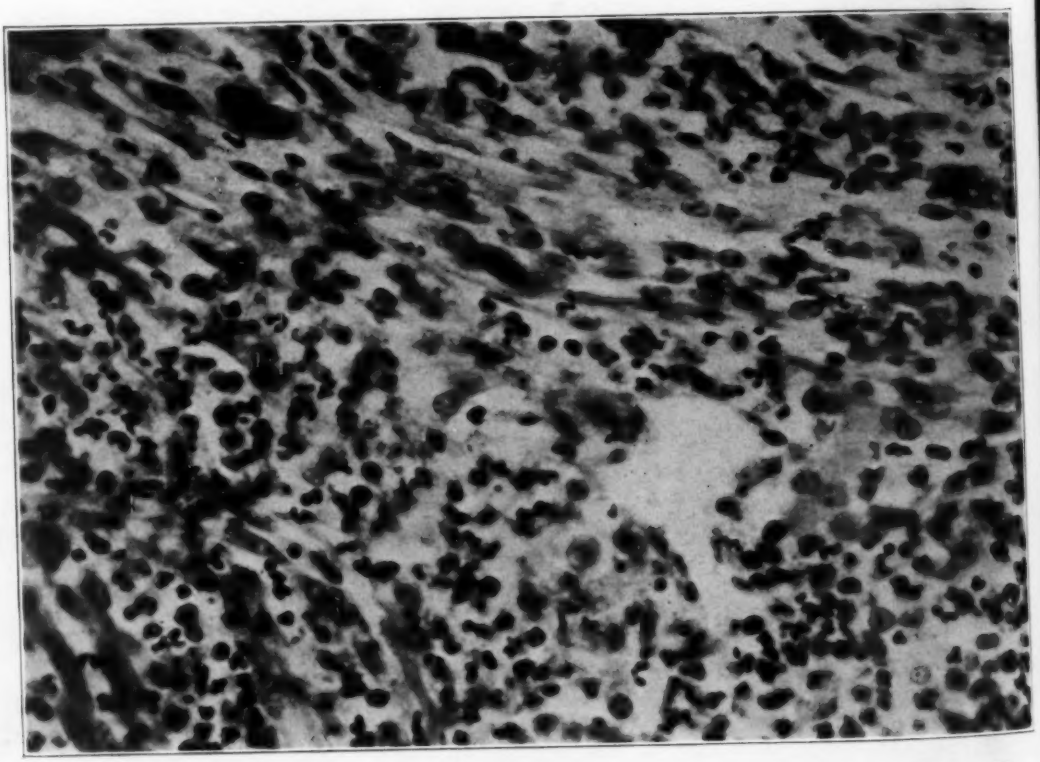

Fig. 8.—Section of the wall of one of the gas-containing abscesses shown in figure 7; × 600. Dense polymorphonuclear infiltration with marked degenerative changes in the hepatic tissues; a tiny gas bubble and bacteria in tissues, both large rods and cocci, are seen. Reduced from a magnification of × 600.

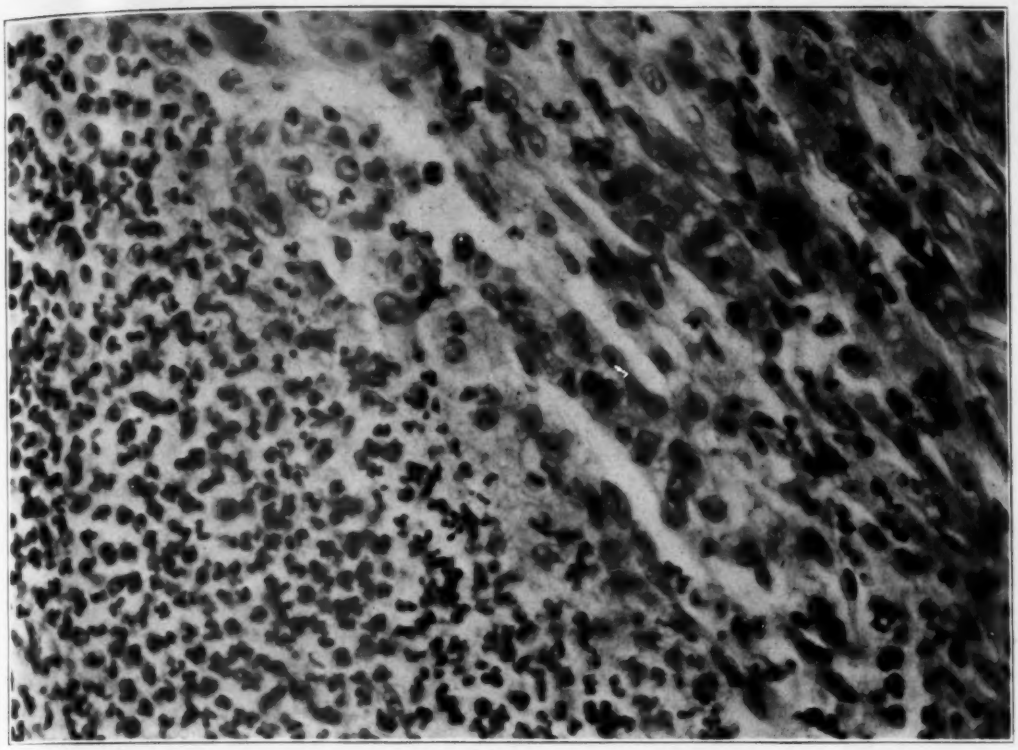

Fig. 9.—Same as figure 8; another field.

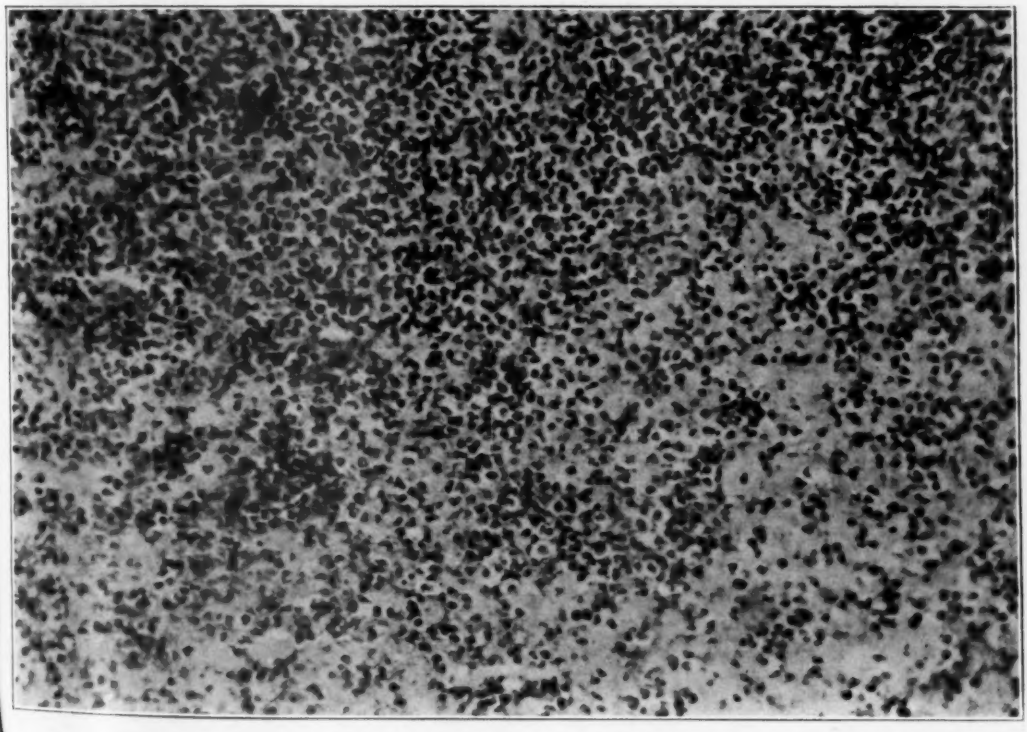

Fig. 10.—Section through muscular walls of the gallbladder four days after ligation of the common and cystic ducts; × 300. Marked cellular infiltration of both round and polymorphonuclear leukocytes is seen. Reduced from a magnification of × 300.

be very dense, and often tiny abscesses are encountered. The infection of the adjacent liver may be extremely severe in time. Even multiple gas-filled abscesses may occur, as shown in figure 7. Examination of the walls of such abscesses shows a dense polymorphonuclear infiltration (figs. 8 and 9) with central necrosis and numerous Welch bacilli as well as cocci in the tissues. The hepatic tissue proper is undergoing marked degeneration. Bile capillaries in the region appear to be con-

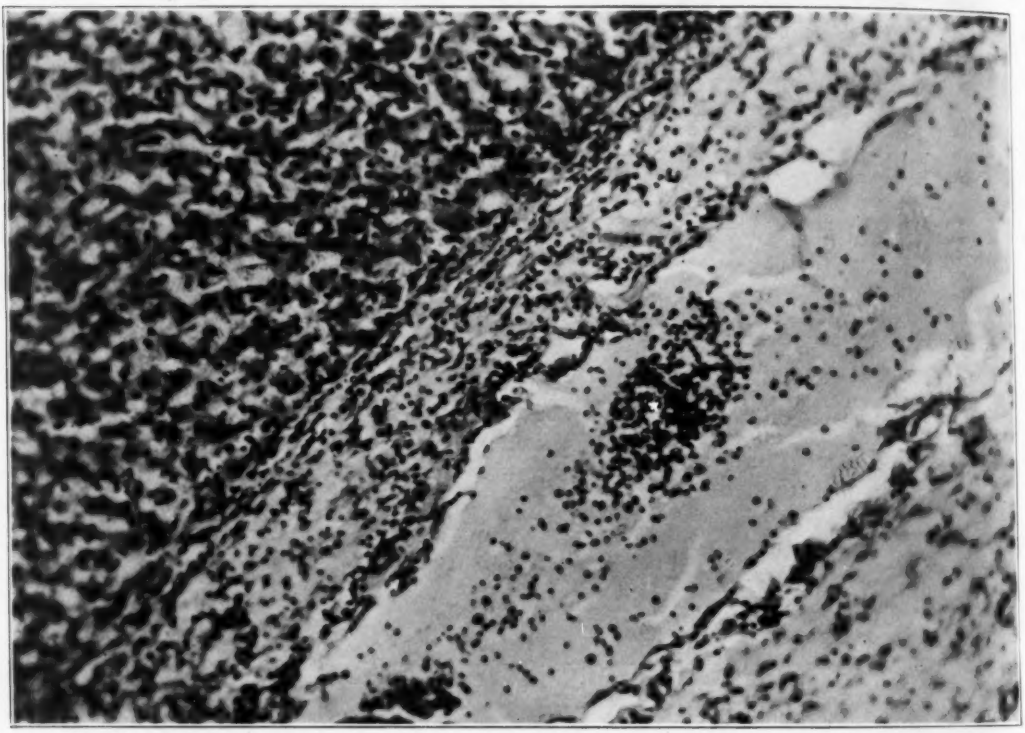

Fig. 11.—Section two months after ligation of the cystic duct; × 180. Note the infiltration of the liver with leukocytes, and the marked edema of the tissues between the gallbladder and the liver with small abscess forming and lesser infiltration of the wall of the gallbladder. Reduced from a magnification of × 180.

spicuously free from involvement in the inflammatory process, as do other parts of the liver.

Infection of the muscular walls of the gallbladder soon takes place. This is manifested by edema (not so marked as in the areolar tissue between the gallbladder and liver) and infiltration of round cells. The polymorphonuclear infiltration is less than in the liver itself in most cases (fig. 10).

As already stated, after ligation of the common duct these changes are not so marked grossly, but histologically they are quite evident. They also begin in the liver and not in the gallbladder.

Figure 11 gives a view of the entire process. The liver shows degenerative change and an invasion of leukocytes. The space between the gallbladder and the liver is markedly edematous and contains a dense localized clump of inflammatory tissue. Leukocytes are also scattered through the edematous area and are beginning to infiltrate the muscular coat of the gallbladder.

COMMENT

The fact that biliary stasis is a factor in the production of cholecystitis has been known for a long time. However, the extent and severity of the accompanying lesions have, I believe, never been called to attention. Walsh and Ivy [10] reported such changes in a recent paper but gave no detailed studies of them. The most important factor is the one here demonstrated that the infection makes it way into the gallbladder by direct extension from the liver, and in the early stages, especially, the characteristic flora is that of the liver. Many of the bacteriologic studies that have been made can be criticized on the basis that special mediums were used in the search for streptococci, and that the anaerobic organisms have not been sought. Ever since Rosenow's reports on the localization of intravenously injected streptococci, these organisms have received special attention. Williams and McLachlan [11] have recovered them from many human cases but could demonstrate no specificity. The elaborate experiments of Wilkie [12] on the production of experimental cholecystitis ignored all other organisms, although in rabbits, the animals they used, the livers contain an especially rich anaerobic flora.

The importance of anaerobes has recently been emphasized by Whitby and Gordon-Taylor.[13] In an extensive review of the literature it is shown that the occasional occurrence of *B. welchii* in series of cultures of the gallbladder in cholecystitis is reported by many observers, although this observation seems usually to be considered as incidental. In their series, anaerobes were found in considerably higher percentages

10. Walsh, E. L., and Ivy, A. C.: Etiology of Gallstones, Ann. Int. Med. **4**:134, 1930.

11. Williams, B., and McLachlan, D. G. S.: Etiology of Cholecystitis, Lancet **2**:342, 190.

12. Wilkie, A. L.: The Bacteriology of Cholecystitis, Brit. J. Surg. **15**:450, 1930.

13. Whitby, L. E. H., and Gordon-Taylor, G.: A Bacteriological Study of Fifty Cases of Cholecystitis, Brit. J. Surg. **18**:78, 1930.

than that reported by previous observers, in 13 per cent of the gallstones and 9.5 per cent of the gallbladders. They emphasize the fact that it is in the acute fulminant or gangrenous gallbladder that *B. welchii* are encountered. The use of antiserum is recommended, and they recognize the probable hepatic origin of such types of cholecystitis, from the known anaerobic flora of that viscus.

Since the publication of their paper, there have been five such cases in the Billings Hospital. The patients were so acutely ill and the sepsis so marked that it was not thought safe to wait for a remission. *B. welchii* was found in three of the cases and in two of these the gallbladder was gangrenous. One died within twenty-four hours after the operation.

The association of hepatitis with disease of the gallbladder has long been known. The localized hepatitis about an inflamed gallbladder often produces an apparent mass of hepatic tissue which overhangs the gallbladder, and which on palpation may be mistaken for that organ. In the French literature this has received a special name, "languette hepatique." The earlier work of Graham also emphasized the fact that the liver took part in infections of the gallbladder. Bits of hepatic tissue excised at operation show marked evidences of infection. The recent report by Flint [14] confirms these observations, and the latter believes that hepatitis is often the result of lesions in the abdomen other than in the gallbladder.

Else [15] has recently given an admirable summary of the evidence that the gallbladder may be secondarily involved from the liver. He demonstrated experimentally the rapid absorption of particulate matter from the retrocholecystic space into the liver. Attention is called to the work of Meyer, Neilson and Feusier [16] showing that enormous numbers of bacteria must be in the circulation to bring about a very high biliary content, and to Graham and Peterman's [17] experiments showing that usually not enough bacteria pass into a normal gallbladder to produce inflammation, but that stasis or injury to the wall of this organ is necessary. From the foregoing data, Else concluded that hepatic cholecystitis by direct extension is of frequent occurrence.

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14. Flint, E. R.: Association Between Gallbladder Lesions and Hepatitis in the Human Subject, Brit. M. J. **1**:1041, 1930.

15. Else, J. E.: The Relationship of Hepatitis to Cholecystitis, Northwest Med. **29**:252, 1930.

16. Meyer, K. F.; Neilson, N. M., and Feusier, M. L.: Mechanism of Gallbladder Infections in Laboratory Animals, J. Infect. Dis. **28**:456, 1921.

17. Graham, E. A., and Peterman, M. G.: Further Observations on Lymphatic Origin of Cholecystitis, Arch. Surg. **4**:23 (Jan.) 1922.

The importance of the liver in the defensive mechanism of the body against infection has been emphasized by Heyd.[18] After abdominal operations, especially septic ones, he warns of the danger of infection of the liver with resulting disturbance of the chemical equilibrium of the body and dwells on the necessity of treating a patient with such a deficiency of the liver by proper chemical means. Mueller and Bruett's [19] experiments on the intravenous injection of bacteria show that the reticulo-endothelial system of the liver is the most active agent in the fixation and destruction of circulating micro-organisms, and that other organs become infected only when they are injured. Petersen and Mueller [20] have shown that the elimination of bacteria from the blood stream is almost stopped after hepatectomy, while Jaffe [21] has demonstrated that particulate matter also continues to circulate in the blood stream after hepatectomy, while it is eliminated in a few minutes by the normal animal.

In this connection, the experiments of Badylkes and Strokow [22] are of great interest. They showed that infection of the gallbladder in animals caused pylorospasm and hyperperistalsis of the small intestines. The obstruction of the pylorus was at times almost complete. The conditions described must approximate accurately those produced by Arnold and Brody [23] in their experiments. They brought a loop of duodenum up under the skin, so that they could inject material into it or aspirate its contents. When the p_H was 8.0 and egg-white was in the duodenum, the lymph from a fistula of the thoracic duct contained from 500 to 1,000 bacteria per cubic millimeter. Such an enormous feeding of bacteria into the circulation must act in such a manner as to keep the liver constantly seeded, especially as it can be shown to occur under conditions likely to obtain in infections of the gallbladder.

The effect of anesthetics on the liver has long been known, especially the lipoid solvent group. Bollman [24] has recently reviewed this subject

18. Heyd, C.: Hepatitis, Surg. Gynec. Obst. **39**:66, 1924; Protective Rôle of the Liver in Abdominal Surgery, Am. J. Obst. & Gynec. **19**:203, 1930.

19. Mueller, E. F., and Bruett, H.: Significance of Liver in Natural Defense Against Infections, München. med. Wchnschr. **76**:2044, 1929.

20. Petersen, W. F., and Mueller, E. F.: Splanchnoperipheral Balance During Chill and Fever, Arch. Int. Med. **40**:575 (Nov.) 1927.

21. Jaffe, R. H.: The Reticulo-Endothelial System, Arch. Path. **4**:45 (July) 1927.

22. Badylkes, S. O., and Strokow, F. Y.: Cholecystitis: Effect on Motor Functioning of Genito-Urinary Tract, Arch. f. Verdauungskr. **47**: 222, 1930.

23. Arnold, L., and Brody, L.: Passage of Living Bacteria Through the Intestinal Wall, Proc. Soc. Exper. Biol. & Med. **25**:247, 1928.

24. Bollman, J. L.: Effect of Anesthetic Agents on the Liver, Proc. Staff Meet., Mayo Clin. **9**:369 (Dec. 18) 1929.

and called attention to the fact that the liver as seen by the surgeon is generally low in glycogen, and that this increases the toxic effect of anesthetics. He advocated ethylene for operation in such cases. Higgins [25] also called attention to the effect of trauma on the liver and found a marked cellular infiltration of the organ. Both of these factors, of course, have an evident bearing on our problem, and in view of the fact that bacteria tend to locate themselves in injured tissue, the importance of such factors in the production of disease of the gallbladder and on the postoperative course in operations on the gallbladder, which involves a field with such a rich flora, may be very great. The recent report of Miller,[26] who advocated operation in many cases of cholecystitis in which most surgeons would attempt medical treatment, seems justified in view of our experimental and clinical observations, as in such severe infections due to *B. welchii* immediate drainage is surely indicated if the condition can be differentiated from the other more mild types.

CONCLUSIONS

1. In biliary stasis the gallbladder of the dog promptly becomes infected with the characteristic anaerobic flora of the liver.

2. Pathologic studies at various stages show that this infection occurs by direct extension from the liver.

3. The fulminant type of human cholecystitis is often caused by the Welch bacillus from the liver.

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25. Higgins, G. M.: Reaction of the Liver to Trauma, Proc. Staff Meet., Mayo Clin. **5**:88 (March 29) 1930.

26. Miller, R. H.: Acute Cholecystitis, Ann. Surg. **92**:644, 1930.

FIBROCARTILAGINOUS TUMORS OF THE BONE*

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The derivation of tissues from more rudimentary antecedents, which is the normal method of achieving adult structures in the human body, constitutes a major source for tumor pathology, since it is in such developmental steps that most neoplasms arise. The structure of the tumor often reveals this fact by a cycle of changes similar in form and sequence to the succesive stages of normal growth in the portion of the body where it arises.

This is well illustrated by the relation of certain tumors of the bone to the evolution and embryologic development of the skeleton. In its primitive form the early vertebrate spine (notochord) is membranous, composed of a cellular connective tissue which is distended with fluid to render this structure resistant to pressure. Later, the notochord becomes cartilaginous, to be replaced in higher forms by a vertebral column and skeleton composed nearly entirely of bone (Darwin,[1] Lull [2]). This transition from connective tissue to cartilage to bone in vertebrate evolution also represents the method by which the human skeleton is formed in the embryo; in addition, this same transition or series of developmental steps is seen in the majority of benign and malignant tumors of bone which are here designated as tumors of the fibrocartilaginous group (fig. 1).

In the present study, over 500 tumors of the skeleton included in this grouping are analyzed, and in their histogenesis it will be shown that these growths repeat, in a concise way, both the evolutionary development and the embryology of this type of tissue. These tumors include the osteochondromas or benign exostoses, the chondromas or chondromyxomas and the chondromyxosarcomas, the latter being a form of osteogenic sarcoma containing cartilage. Taken broadly, these three groups of lesions represent different stages of the same pathologic process and may be graded from the more primitive and malignant to the more highly differentiated and benign—the most primitive, the chondromyxosarcoma, being malignant, the chondromas being potentially malig-

* Submitted for publication, Sept. 25, 1930.

* Illustrations by Mr. Herman Schapiro.

* From the Surgical Pathological Laboratory, Johns Hopkins Hospital and University.

1. Darwin, C.: Origin of the Species, ed. 1, London, J. Murray, 1859.

2. Lull, R. S.: Organic Evolution, New York, The Macmillan Company, 1927, p. 460.

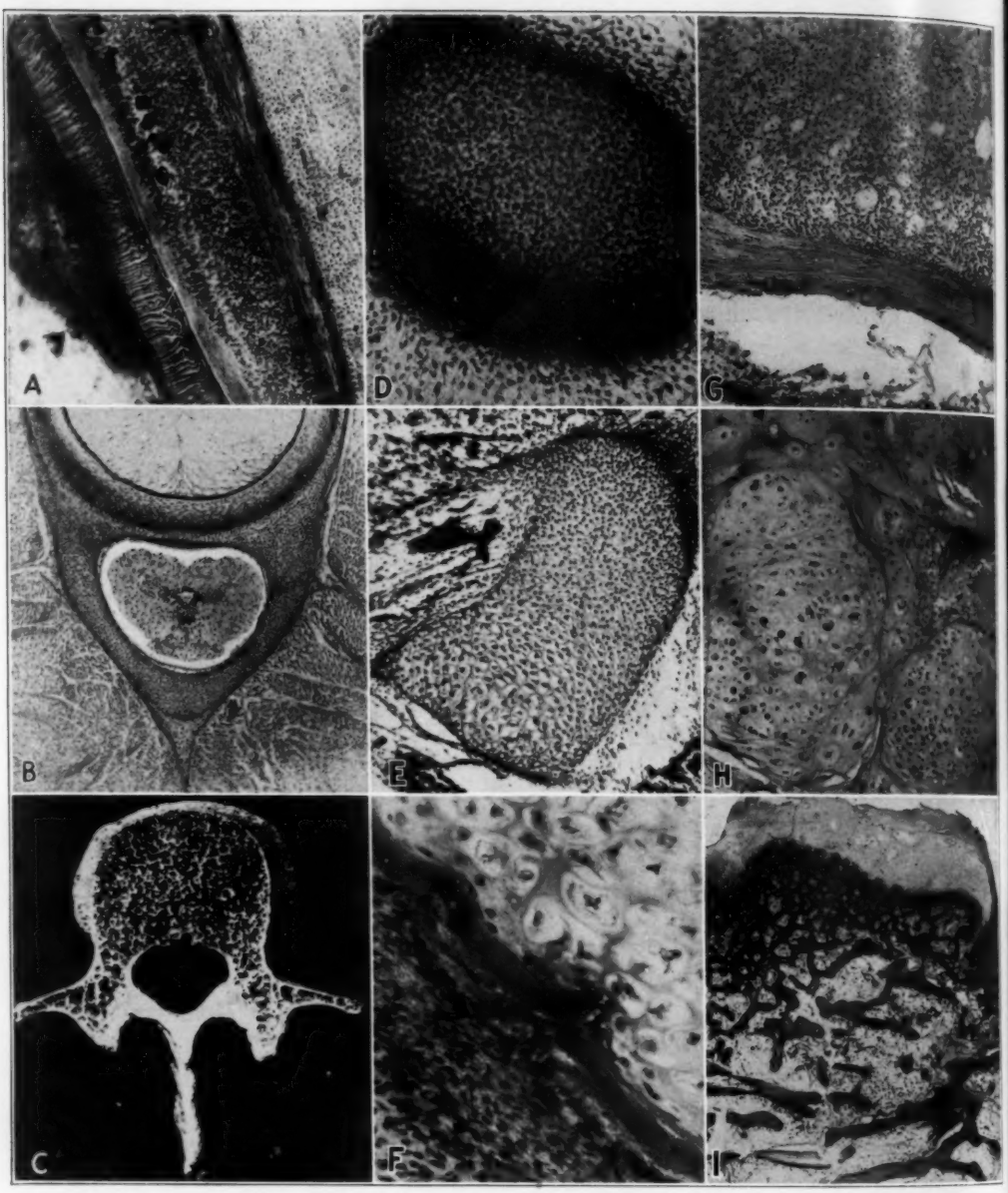

Fig. 1.—Comparison of the cycle of development in skeletal tissues in evolution (*A, B, C*) in the embryo (*D, E, F*) and in tumors of the fibrocartilaginous group (*G, H, I*). *A*, a longitudinal section of the membranous spine or notochord of the amphioxus, one of the most primitive of the vertebrates; *B*, the essentially cartilaginous structure of the vertebrae in the dog fish, an animal well along in the scale of evolution of the vertebrates; *C*, the osseous structure of the adult vertebrae in man; *D*, the first step in the formation of the skeleton in the human embryo, with primitive connective tissue or mesenchyme condensing at the site of the future skeleton; *E*, the early formation of cartilage from primitive connective tissue in the human embryo; *F*, a rim of permanent bone being laid down about calcified cartilage which is being resorbed by giant cells, one of which is shown in the picture. This is the final stage of ossification on the human embryo. *G* shows the microscopic appearance of a chondromyxosarcoma at the margin of the tumor. The neoplastic tissue is a proliferation of embryonic connective tissue and fetal cartilage cells or so-called myxoma. *H* shows the essentially cartilaginous structure of a benign chondroma, and *I*, the predominantly osseous structure of a benign osteochondroma.

nant in their recurrent form and the osteochondromas being essentially benign. Histologically also, there is no sharp dividing line between these three forms of neoplasms, since the basic tissues comprising them, connective tissue, cartilage and bone, are present in varying amounts in all of these growths.

OSTEOCHONDROMAS

The osteochondromas, or exostoses, are benign tumors, usually occurring in persons between the ages of 10 and 25 years near the end of the long bones and forming bony skeletal outgrowths with a thin cartilaginous cap. The symptoms are generally mild and of long duration, averaging over five years. The roentgenogram of the involved bone gives a typical picture in which the characteristic features are a base or pedicle, springing directly from the cortex of the underlying bone without an intervening zone of abnormal osseous tissue and with an overlying expanding cap composed of cartilage undergoing calcification or ossification. Microscopic examination of the excised tumor reveals normal laminated bone beneath a transitional zone of calcifying cartilage which is overlayed by a thin strand of fibrous tissue. Histogenetically, it will be shown, these tumors are an exaggeration of a normal bony protuberance intended for the anchoring of an important tendon.

CLINICAL FEATURES

While the roentgenogram and the microscopic section of an osteochondroma usually present fairly uniform changes, many of the clinical features of this lesion are notably variable. This type of skeletal outgrowth which is generally contiguous with the bone, but which rarely may be entirely separated from it and embedded in the substance of a tendon or of a soft part structure, is associated with many different etiologic factors. Some of these tumors are undoubtedly congenital; in addition, there is a distinct familial history. Cases in which several members of the same family in one or more generations are affected by multiple outgrowths of the exostosis type are by no means rare (Ehrenfried[3]). At the opposite extreme, development of a type of tumor identical in histologic structure with such congenital exostoses may take place in adult life as the result of chronic infection, the calcaneal spurs in chronic gonorrheal arthritis being a common example.

This variability of etiologic factors is reflected in the age incidence of the disease, for while osteochondromas are essentially a neoplasm of the early decades with the peak of the curve of age incidence between 10 and 20 years, about 30 per cent are observed in patients over 30

3. Ehrenfried, A.: Hereditary Deforming Chondrodysplasia; Multiple Cartilaginous Exostoses: A Review of the American Literature and Report of Twelve Cases, J. A. M. A. **68**:502 (Feb. 17) 1917.

years of age (fig. 2). Those exostoses in patients under 30 are either congenital or traumatic and rarely infectious (due to gonorrhea contracted during the postadolescent period). After the age of 30, infection plays a greater rôle in the onset of the growth, the various types of chronic arthritis being responsible for a definite group of these tumors occurring in adults. The types of exostoses occurring early in life, congenitally or traumatically, also may be recorded in patients well over 30, since the absence of symptoms often permits a latent period of over twenty-five to forty years. This tendency of osteochondromas to remain latent or

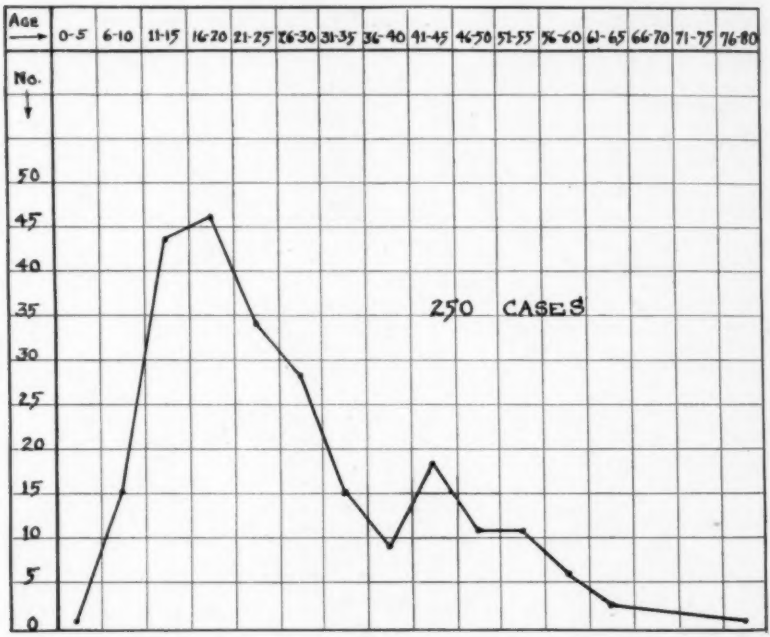

Fig. 2.—Chart showing the age incidence of benign osteochondromas, or exostoses.

evade clinical observation is shown by the fact that although 25 per cent of these lesions apparently date from birth, only 6 per cent are observed clinically in patients less than 10 years of age.

Figure 3 shows the skeletal distribution of these exostoses. In analyzing the distribution of these tumors, it was found that nearly twice as many males were affected as females and that whites predominated, only 16 colored patients being present in this series of 262 cases. Nearly one third of the tumors occurred about the knee joint in the lower end of the femur or upper end of the tibia. The majority of the remaining tumors were located at the ends of the long bones of the ankle, the shoulder, the hip or the elbow. The other sites of importance are the

region of the jaw and skull and the small bones of the foot or hand. It must be borne in mind, however, that tumors of the skull and jaws often grouped under exostoses are, properly speaking, osteomas, representing a different type of ossification in fibrous tissue, and that some of the tumors of the small bones of the hand and feet either fall into this category or are related to aberrant sesamoid bones.

The striking feature of the skeletal distribution of osteochondromas is their periarticular location and their relation to sites of tendinous

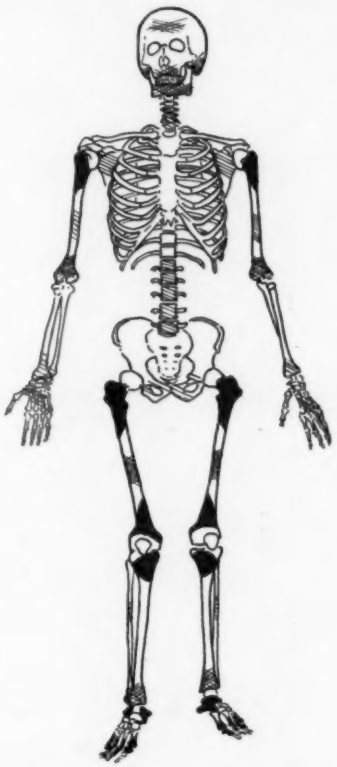

Fig. 3.—Incidence of osteochondroma according to skeletal location. The solid black areas indicate the most frequent sites; the checked areas, the common sites; the diagonal lines, the occasional or rare locations.

attachments. These tendons are generally those involved in regions of maximal traction, being at the ends of such muscles as the adductor magnus and quadriceps femoris in the thigh and the gastrocnemius and soleus at their convergence in the Achilles tendon. A further peculiarity of these sites is the fact that the tendons attach not to the periosteum but directly to the bone.

The average duration of symptoms for the cases of osteochondroma listed in table 1 is sixty-one months, or slightly over five years. This

TABLE 1.—*Benign Osteochondromas (Exostoses)*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment‡
44619*	C	M	18	Tibia, left	4	Pain; tumor	Multiple pedicle exostoses	Excision, Jan. 21, 1929	New bone	Discharged well
44257	W	F	45	Femur, external condyle	..	Fracture; pain	.....	Excision, November, 1928	Cancellous bone; old cartilage	Discharged well
43691	W	F	56	Toe	..	.....	.....	Removal of toe	.....	Discharged well
43549	W	M	16	Tibial tuberosity	72	Trauma; pain; tumor	Bursa over exostosis with cartilaginous cap	Exploration	Cancellous bone; adult cartilage	Discharged well
43497	W	M	14	Femur, lower right	12	Trauma; pain; tumor	.....	Excision, June, 1928	Cancellous bone; adult cartilage; some fetal cartilage	21 mo. well
43347	W	M	18	Toe, left	..	.....	.....	Excision, May, 1928	Cancellous bone; old cartilage	Discharged well
43185	W	M	40	Thumb, left	..	.....	Rounded exostosis	Excision, March, 1928	Cancellous bone; adult cartilage; some new bone	Discharged well
43095	C	F	22	Jaw, lower	96	Tumor; deformity of mouth	.....	Excision, March, 1928	Cancellous bone; old cartilage	Discharged well
43042	W	M	20	Fibula	..	Pain; tumor	Broad exostosis; cartilaginous cap	Excision, June, 1930	Calcifying cartilage; osteoid tissue	.....
42797	W	F	18	Skull, frontal	144	Trauma; tumor	Rounded exostosis	Excision, February, 1928	Cancellous bone	Discharged well
42142	W	M	11	Tibia, upper, left	..	Tumor	Cystic periosteal shadow	.....	.....	.....
41825	W	M	19	Foot, dorsum	48	Trauma; pain; tumor	Rounded exostosis over joint	Exploration, Aug. 1, 1927	Cancellous bone; adult cartilage	Discharged well
41563	W	M	18	Femur	..	.....	.....	Excision, June 24, 1927	Cancellous bone; adult cartilage	Discharged well
41519	..	F	15	Toe, right foot	..	.....	.....	Excision, June 18, 1927	Cancellous bone	33 mo. well
41267	W	M	39	Femur and tibia	..	.....	.....	Excision, May 2, 1927	Cancellous bone, adult and calcified cartilage	Discharged well
41260	W	F	62	Foot, second metacarpal	2	Trauma; pain	Bone formation with transverse fracture	Biopsy	Cancellous bone	1 yr. well
40896	W	M	13	Tibia, lower end	9	Trauma; pain; tumor	Rounded exostosis	....	.....	.....
40702	W	F	9	Humerus, upper end	5	.....	Rounded exostosis, cystic	No operation	.....	20 mo. well
40652	W	M	20	Fibula and tibia	96	Tumor	Rounded exostosis, cystic	No operation	.....	.....
40648	W	M	..	Humerus, upper	9	Tumor	Cystic periosteal shadow	No operation	.....	Well 29 mo.
40545†	W	M	15	Femora, multiple	180	Congenital tumors; abnormal gait	.....	Excision, January, 1927	Cancellous bone; calcified cartilage	Discharged improved
40523	W	M	20	Humerus	..	Tumor	.....	Excision, January, 1927	Cancellous bone; adult cartilage	Discharged well

40352	W	F	..	Femur, lower end	..	.....	.....	Excision, March, 1928	.....	1 mo. well
40250	W	M	40	Femur, lower third	420	Trauma; tumor	Pedicle exostosis	Excision	Cancellous bone	2 yr. well
40071	W	F	50	Toe, left foot	..	.....	.....	Excision, October, 1926	Cancellous bone; adult cartilage	Discharged well
40040	W	M	14	Femur, interior shaft	24	Tumor	Pedicle exostosis	Excision, Jan. 24, 1928	Cancellous bone; adult cartilage	2 yr. well
39835	..	M	43	Palate, hard	..	.....	.....	Excision	Cancellous bone	Discharged well
39916	W	F	11	Humerus, upper third	24	Pain; tumor	Pedicle exostosis	No operation	.....	2½ yr. well
39782	W	F	6?	Radius, lower	60	Tumor	Pedicle exostosis	No operation	.....	2 yr., condition unchanged
39502	W	F	11	Femur, lower	1	Tumor	Broad exostosis; cartilaginous cap	Excision, July, 1927	Cancellous bone; adult cartilage	2½ yr. well
39472	W	M	19	Femur, lower	120	Tumor	Broad exostosis; cartilaginous cap	Excision	Cancellous bone; calcified cartilage	2½ yr. well
39445	W	M	41	Ileum, lip, right, acetabulum	36	Pain; tumor	.....	Excision, June 9, 1926	Cancellous bone	Discharged well
39443	W	F	56	Femur, right, internal condyle	..	.....	.....	Excision, June, 1926	Cancellous bone; old cartilage	3½ yr. well
39421	W	M	45	Maxilla, right	18	Tumor	Obliteration of antrum	Excision, June, 1926	Cancellous and new bone	Discharged well
39405	W	F	35	Maxilla, right	..	.....	Obliteration of antrum	Excision, June, 1926	Cancellous and new bone	Discharged well
39173	W	F	16	Femur, left	..	.....	.....	Excision, April, 1926	Cancellous bone; adult	Discharged well
39064	W	F	30	Femur, upper, left	18	Pain; tumor	Cauliflower exostosis	None	.....	.....
38845	W	F	55	Jaw	..	.....	Rounded exostosis	Excision, March, 1926	New bone	Discharged well
38784	W	F	10?	Scapula, right	6	Tumor	Pedicle exostosis	Excision	Cancellous bone; adult cartilage	2½ yr. well
38780	W	M	45	Femur, lower	..	.....	Pedicle exostosis	.....	.....	Well, 1929
38694	W	F	..	Fibula, upper	..	.....	Broad exostosis; cartilaginous cap	.....	.....	Well, 1928; lost
38613*	W	M	28	Femur, right; fifth lumbar vertebra	96	Trauma; pain; tumor	.....	Excision, 1926, 1928	Cancellous bone; adult cartilage	2 yr. well
38466	W	M	28	Os calcis	..	.....	Pedicle exostosis in achilles' tendon	Excision, 1923	.....	Well, 1929
38460	W	M	12	Humerus, upper	¼	Tumor	Broad exostosis; cartilaginous cap	.....	Cancellous bone; calcified cartilage	Discharged well
38215	W	F	40	Jaw, left, lower	..	.....	.....	Excision, November, 1925	Cancellous bone; adult cartilage	Discharged well
37582	W	F	18	Humerus, shaft	4	Tumor; pain	Broad exostosis; cartilaginous cap	Excision, February 1926	Cancellous bone; adult cartilage	4 yr. well
37549*	W	F	30	Humerus, left upper tibia, fibula, right	252	Tumor	.....	Excision, 1925	Cancellous bone; adult cartilage	Discharged well
37373	W	M	18	Humerus, upper, right	6	Trauma; tumor	Broad exostosis	Excision, May, 1925	Cancellous bone; adult cartilage	.....
37365	..	F	31	Toe, right, little	12	Tumor	.....	Excision, May, 1925	Cancellous bone	Discharged well
37262	W	F	20	Tibia, lower	½	Pain	Broad exostosis; cartilaginous cap	Excision, November, 1925	.....	Discharged well

* Cases of multiple exostoses.
† Cases with typical hereditary, deforming chondrodysplasia in which more than one member of the family was affected.
‡ The results of treatment shown have been figured from the date of the first operation.

TABLE 1.—*Benign Osteochondromas (Exostoses)—Continued*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment
37158*	W	M	21	Tibia, upper; upper right and left fibula	..	.....	Multiple pedicle exostosis	.....	.....	Discharged well
36752	W	F	14	Fibula, left, upper	8	Pain	Broad exostosis; cartilaginous cap	Excision, manipulation, July, 1925	Cancellous bone	5 yr. well
36666	C	M	42	Knee, left	6	Trauma; pain; tumor	Hypertrophic arthritis	Exploration	.....	Lost
36642	W	M	12	Jaw, lower left	3	Tumor; pain	.....	Excision	.....	5 yr. well
36521	W	F	39	Skull, right and frontal	48	Tumor	Rounded exostosis	Excision, December, 1924	Cancellous bone; dense fibrous tissue	5 yr.; no recurrence
36402*	..	M	9	Tibia, shaft; femur, upper and lower	12	Bowing; slight trauma	Metaphyses widened and deformed	Straightening fracture	.....	.....
36189	..	..	16	Arm	..	Trauma	Pedicle exostosis; cartilaginous cap	Excision	Cancellous bone; old cartilage	Discharged well
35867	W	F	11	Humerus, right	48	Tumor	.....	Excision	Cancellous bone; old cartilage	5½ yr. well
35831	W	F	15	Toe, right, middle	..	.....	.....	Excision	Cancellous bone beneath normal nail-bed	6½ yr. well
35826	W	M	33	Tibia, internal condyle	60	Tumor; pain	Broad exostosis	.....	.....	.....
35760	W	M	29	Femur, lower, left	6	Trauma	Broad exostosis; cartilaginous cap	Excision	Fibrous tissue	Discharged well
35720	W	M	15	Tibia, upper	24	Trauma; tumor	Pedicle type with bursa	Excision	Cancellous bone; adult cartilage	Well over 1 yr.
35718	W	F	15	Femur, shaft	12	Tumor	Broad exostosis; cartilaginous cap	.....	.....	.....
35714	W	M	10	Femur, shaft, lower third	48	Trauma; tumor	Pedicle exostosis; cartilaginous cap	Excision	Cancellous bone; adult cartilage; many giant cells	Discharged well
35712	W	F	16	Tibia, shaft, left internal condyle	48	Tumor	Broad exostosis; cartilaginous cap	.....	.....	5½ yr. well
35661	W	M	24	Toe, large left; distal phalanx	168	Tumor	.....	Excision, June, 1924	Cancellous bone; fetal adult and calcified cartilage	Discharged well
35624*	..	M	..	Fibula, upper; tibia, upper	..	Tumor; pain	Metaphyses widened and deformed	.....	.....	Lost
35382*	W	M	19	Tibia, upper and lower; fibula; ulna	48	Tumors; multiple	Multiple pedicle exostosis, metaphyses widened	.....	.....	.....
35380	..	M	..	Femur, left lower	36	Trauma	Broad exostosis; cartilaginous cap	.....	.....	5½ yr. well
35366	W	F	18	Tibia, left, lower external	24	Tumor; pain	Broad exostosis;	Excision, June, 1924	.....	5½ yr. well
35237	W	M	21	Os calcis, right	..	.....	.....	Excision, April, 1924	Cancellous bone	Discharged well
35108	..	F	5	Temporal bone	..	.....	Area of bone destruction under rounded exostosis	.....	.....	6 yr. well

35010	W	M	23	Radius, upper, right	6	Pain	Cystic tumor	Curettement, 1924	.....	.....	
34605	W	F	46	Os calcis, left	12	Tumor; pain	.....	Excision, February, 1924	Cancellous bone; adult cartilage	6 yr. well	
34436	W	M	17	Femur, shaft	2	Trauma	Flat, broad, ossifying periostitis	.....	.....	6 yr. well	
34244	W	M	50	Auditory canal, external	10	Tumor	.....	Not advised	.....	.....	
34167	W	M	39	Os calcis	..	.....	.....	Operation, October, 1923	Cancellous bone; adult cartilage	Discharged well	
33986	W	F	23	Skull, right	172	Tumor; pain	Rounded exostosis	No operation	.....	.....	
33944	W	M	12	Tibia, left, upper	15	Tumor	Pedicle exostosis; cartilaginous cap	Excision, August, 1924	Cancellous bone	5½ yr. well	
33926	W	M	..	Humerus, external condyle	..	Tumor	Rounded exostosis	Excision, September, 1923	Cancellous bone; adult cartilage	Discharged well	
33750	W	F	18	Femur, lower	24	Trauma; tumor	Broad exostosis; cartilaginous cap	No operation	.....	.....	
33533	W	M	19	Humerus, mid-shaft, right	228	Congenital tumor	Periosteal cauliflower mass	Excision, August, 1922	Adult cartilage; cancellous bone	Well 7 yr.	
33168	W	M	13	Humerus, upper, right	..	Tumor; fracture	Fracture through pedicle exostosis	Excision ?	.....	6½ yr. well	
33155	W	M	30	Femur, lower, right	24	Tumor; trauma; pain	Pedicle exostosis; cartilaginous cap	Excision, 1915, 1923	Calcified cartilage; adult cartilage; myxoma	Recurred; well, 1924	
32889	W	M	30	Pubis	..	Trauma; tumor	Rounded exostosis	.....	.....	.....	
32664	W	M	44	Scapula	18	Pain	Periosteal translucent area; rarefaction beneath	Exploration, April, 1923	Adult cartilage	Well 7 yr.	
32545	W	M	43	Pubis, left	4	Trauma; tumor	Broad exostosis; cartilaginous cap	No operation	.....	Tumor larger, 7 yr.	
32538	W	M	22	Femur, lower, right	36	Trauma; tumor; pain; limping	Rounded exostosis	.....	.....	Lost	
32494	W	F	56	Ulna, styloid	72	Tumor	Sesamoid bone ?	Operation refused	.....	7 yr. well	
32357	W	M	13	Skull	..	Tumor	Rounded exostosis	Excision, February, 1923	.....	Discharged well	
32317	W	M	25	Femur, shaft, right	18	Trauma; tumor; pain	Large periosteal calcifying mass	Exploration, January, 1923	Adult cartilage; cancellous bone	Well 3 mo.	
32267	W	M	62	Femur, shaft	..	Pain; stiffness	Pedicle exostosis	No operation	.....	7 yr. well	
32020	W	F	46	Femur, lower	192	Trauma; tumor; pain	First, ossifying tumor; second, osteophytes in stump	Amputation, 1916; disarticulation, 1923	New bone; adult cartilage	Recurred; well, 1926	
31932	W	M	6	Humerus, upper, left	..	Tumor	Broad exostosis	Biopsy, 1923	Hyaline cartilage and cancellous bone	Well 5 yr.	
31794	W	F	28	Humerus, upper	144	Trauma; tumor	Large periosteal translucent area	Cauterized, 1922; excised, 1924	Cancellous bone; adult cartilage	Well 6 yr.	
31522	W	F	14	Femur, lower	36	Trauma; tumor	Pedicle exostosis; cartilaginous cap	Exploration	Cancellous bone	6 yr. well	
31132	W	M	17	Femur, lower, right	16	Tumor; pain	Pedicle exostosis	.....	.....	Well 8 yr. after onset	
31064	W	M	16	Femur, lower, right	12	Tumor	Pedicle exostosis	.....	.....	.....	

TABLE 1.—*Benign Osteochondromas (Exostoses)—Continued*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment
30690	W	M	30	Metatarsals, fourth and fifth, right	180	Trauma; tumor; pain	Rounded exostosis	Excision, June, 1922	Cancellous bone	Discharged well
30568*	W	F	28	Femur; tibia; fibula	192	Tumor; tenderness	Multiple pedicle exostosis	Excision	Cancellous bone; adult cartilage	Well over 7 yr.
30453	W	M	18	Tibia, upper, left	..	Pain	Pedicle exostosis	Excision	.....	.....
30452	W	M	24	Femur, lower, right	72	Trauma; tumor	Pedicle exostosis	.....	.....	.....
30451	W	M	24	Femur, lower, right	60	Tumor	Broad exostosis	.....	.....	.....
30450	W	M	19	Femur, lower, right	18	Trauma; pain; stiffness; familial	Pedicle exostosis	.....	.....	.....
30449	W	M	21	Femur, lower, right	..	Pain; tumor	Pedicle exostosis	.....	.....	.....
30436	W	M	30	Humerus, lower, left	..	Tumor	Pedicle exostosis	Incised, March, 1922	.....	7 yr. well
30398*	W	M	..	Frontal bone, right; clavicle, right; maxilla, left	..	Syphilitic history	Multiple rounded exostosis	Antisyphilitic, 1922	.....	Exostosis disappeared
30383	W	F	34	Occiput	12	Tumor	Broad exostosis	.....	.....	Unchanged 6 mo.
30304	..	M	..	Femur; trochanter; left	42	Pain	.....	Excision, February 1922	Cancellous bone; adult cartilage	Discharged well
30265	W	M	16	Second metatarsal, right	½	Tumor	.....	Excision, May, 1922	.....	Discharged well
30186	W	M	40	Femur, upper	..	Tumor	.....	Amputation, October, 1917	.....	Well 5 yr.
30183	W	M	11	Humerus, upper, left	½	Tumor	Rounded exostosis	Resection, June, 1919	.....	Well over 10 yr.
30173	W	M	15	Lumbar, first	24	Pain	Periosteal translucent area	Excision, September, 1915	Cancellous bone; adult cartilage	Well 14½ yr.
30129	W	F	80	Scapula	3	Pain; limitation of motion	.....	.....	.....	8 yr. well
30109	W	M	37	Humerus, greater tuberosity	36	Pain; limitation of motion	Broad exostosis	No operation	.....	Condition unchanged
30045	W	M	18	Humerus, upper, left	..	Tumor	Broad exostosis	Excision, March, 1922	.....	Discharged well
29832	B	M	..	Humerus, lower, left	..	Tumor	.....	Excision, March, 1922	.....	Discharged well
29747	W	M	21	Ulna, lower	144	Tumor; limitation of motion	.....	Excision, April, 1922	.....	Discharged well
29664	W	M	..	Femur, neck, left	36	Trauma; pain; limitation of motion	Broad fuzzy exostosis	Excision, 1921; 1922	Cancellous bone; adult cartilage	Recurred, well 9 yr.
29638	C	M	30	Femur, neck	36	Trauma; pain; stiffness	.....	.....	.....	Lost
29455	W	F	54	Index finger, right terminal phalanx	..	Trauma; pain	Rounded exostosis	Excision, January, 1922	.....	8 yr. well
29154*	W	F	30	Tibia; fibula; humerus	..	Tumors	Multiple pedicle exostosis	No operation	.....	Unchanged 8 yr.

29009	W	..	16	Femur, upper	36	Trauma; tumor	Broad exostosis	.....	.....	.....
28992	W	M	33	Femur, lower, right	48	Trauma; pain; adductor spasm	Broad fuzzy exostosis	Excision, September, 1921	Cancellous bone; adult cartilage	Well almost 9 yr.
28865	W	F	12	Tibia, upper	36	Trauma; tumor	Broad exostosis; cartilaginous cap	Excision, September, 1921	Cancellous bone; adult cartilage	Well almost 8 yr.
28701	W	M	11	Tibia, lower, right	..	Tumor	Broad exostosis; cartilaginous cap	Excision, September, 1921	Cancellous bone; adult and fetal cartilage; myxoma in tendon	Well 9 mo.
28665	C	M	18	Femur	..	Tumor	.....	Excision, August, 1921	.....	Discharged well
28601	W	M	36	Femur, shaft	312	Trauma; tumor	Pedicle exostosis	No operation	.....	Condition unchanged
28596	C	M	50	Humerus, right	..	Tumor	.....	Excision, July, 1921	.....	Discharged well
28539†	W	M	9	Femur, lower and upper; fibula	..	Tumors	Multiple broad exostosis	No operation	.....	Unchanged 9 yr.
28225	W	F	20	Skull, frontal	228	Trauma; tumor; pain; strabismus	Rounded exostosis	Excision, May, 1921	Cancellous and new bone	Well 1 yr.
28062	W	M	11	Humerus, upper	36	Tumor	Broad exostosis; cartilaginous cap	Excision, 1921	Cancellous bone	Well 3 yr.
27937	W	F	11	Clavicle	12	Trauma; tumor	Rounded exostosis	Resection, May, 1910	.....	Well almost 20 yr.
27816	W	M	23	Humerus, upper, right	24	Tumor; pain	Rounded exostosis	No operation	.....	Condition unchanged
27697	W	M	28	Femur, lower	240	Trauma; tumor	Pedicle exostosis	No operation	.....	Condition unchanged
27508	W	M	18	Humerus, shaft	42	Trauma; tumor; pain	.....	Excision, 1920	.....	Well 6 yr.
27228	W	M	..	Phalanx, second	..	Tumor	Rounded exostosis	No operation	.....	Condition unchanged
27218	C	M	23	Os calcis	..	Gonorrheal arthritis	Calcaneal spurs	Excision, 1920	Cancellous bone; adult cartilage	Discharged well
27194	W	M	10	Femur, left	..	Tumor	.....	Excision, December 1920	Cancellous bone; adult cartilage	Discharged well
27157	W	M	11	Fibula, head	..	Tumor	.....	Excision, November, 1920	Cancellous bone; adult cartilage	1 yr. well
27079	W	F	19	Ilium	6	Tumor; pain	Fuzzy broad exostosis	Excision, April, 1910	New bone	20 yr. well
27051	C	F	17	Tibia tuberosity	36	Trauma; pain	Broad exostosis	Excision, November, 1920	Cancellous bone	Discharged well
26784*	W	M	11	Radius, lower; humerus, upper	132	Tumors	Multiple pedicle exostosis	No operation	.....	Condition unchanged
26738	W	M	28	Skull, frontal	276	Trauma; tumor; pain	Rounded exostosis	Excision, 1912; 1914; 1920	Cancellous bone	Repeated recurrences
26656	W	M	21	Navicular, right wrist	4	Trauma; tumor; pain	.....	Excision, August, 1920	Cancellous bone; adult and calcifying cartilage	9½ yr. well
26640†	W	F	10	Multiple	..	Tumors	Multiple pedicle exostosis	Biopsy	.....	Condition unchanged
26583	W	M	19	Mastoid	36	Tumor; pain; deafness	.....	Excision, August, 1920	Cancellous bone; cellular fibrous tissue	Well almost 10 yr.
26423	W	M	33	Skull, frontal	84	Trauma; tumor	.....	Excision, July, 1920	New bone; fibrous tissue	Well 1 yr.
26392	W	F	14	Fibula, upper, right	36	Tumor; pain	.....	Excision, July, 1920	Cancellous bone; fetal and adult cartilage; myxoma	Discharged well
26285	W	M	19	Femur, lower	48	Tumor	Pedicle exostosis	Excision, 1910; 1920	Cancellous and new bone	Recurrence, well 10 yr. after second operation

TABLE 1.—*Benign Osteochondromas (Exostoses)—Continued*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment
26272	W	F	55	Humerus, right	36	Trauma; pain; stiffness	.....	Excision, June, 1920	Cancellous bone	Well 9½ yr.
26120	W	F	59	Femur, upper, right	300	Infection	.....	Excision, May, 1920	Cancellous bone	.....
26097	W	M	51	Femur, upper, right	..	Tumor	.....	Excision, 1920	Cancellous bone and adult cartilage	Discharged well
26059	W	F	47	Astragalus, right	..	Tumor	.....	Excision	Cancellous bone and adult cartilage	Walking almost impossible after 10 yr.
25955	W	M	10	Os calcis	14	Pain	Rounded exostosis	Excision	Cancellous bone and adult cartilage	Discharged well
25852	W	M	49	Radius, head	..	Tumor	.....	Excision, March, 1920	Cancellous bone and adult cartilage	Discharged well
25802	W	M	11	Third lumbar vertebra, transverse process	27	Pain; tumor; stiffness	.....	Excision, March, 1920	Cancellous and new bone	Discharged well
25432*	W	F	13	Humeri; fingers; tibiae	132	Multiple tumors	Multiple pedicle and broad exostosis	No operation	.....	Condition unchanged
25128	W	M	47	Fifth lumbar vertebra	12	Pain on standing	.....	Excision, October, 1919	Cancellous bone	Well 10 yr.
24988	W	M	19	Tibia tuberosity	24	Tumor	.....	.....	.....	.....
24432	W	M	12	Tibia, upper	24	Tumor; pain	Expanded, rarefied, subcortical area	Excision, April, 1919	Adult and calcifying cartilage	Discharged well
24212	W	F	19	Navicular, left foot	33	Fracture; tumor; pain	Fracture through exostosis	.....	.....	.....
24014	W	M	32	Os calcis	48	Gonorrheal arthritis; pain	Calcaneal spurs	Excision, January, 1919	Cancellous bone in tendon	Discharged well
24003	W	F	24	Spine	48	Pain	Overgrowth in Albee transplant	Excision, May, 1922	Cancellous bone in tendon	Discharged well
23886	W	M	30	Phalanx, little finger	..	Tumor	Pedicle exostosis	Excision, 1918	Cancellous bone; adult cartilage	Well 1 yr.
23885	W	M	21	Tibia, upper	72	Tumor	Broad exostosis	Excision, December, 1916	Cancellous bone; adult cartilage	Well 5 yr.
23767	W	M	45	Femur, neck	24	Pain; limitation of motion; gonorrheal history	Broad exostosis	Excision, November, 1918	Cancellous bone; calcified cartilage	Discharged well
23599	W	F	27	Spine	12	Paraplegia	.....	Excision, 1918; 1925	New bone	Died, 1926; decubitus ulcers
23583	W	M	16	Humerus, lower	14	Fracture; tumor; limitation of motion	Exhuberant callus	Excision, August, 1918	Cancellous bone	Discharged well
23438	W	M	26	Big toe, right	60	Trauma; tumor	Broad exostosis	Excision, July, 1918	.....	Lost
23395	W	F	10?	Humerus	..	Tumor	.....	Excision, July, 1918	.....	.....
22907	W	F	43	Femur, left head	8	Pain; limitation of motion	.....	Excision, March, 1919	Cancellous bone in tendon	Well almost 21 yr.
22827	W	M	23	Os calcis, left	3	Gonorrheal arthritis	Calcaneal spur	Excision, February, 1917	Cancellous bone; calcifying cartilage in tendon	Discharged well

22733	W	M	19	Os calcis	..	Pain	Calcaneal spur	Excision, January, 1918	Calcified cartilage in tendon, myxoma	12 yr. well
22306	W	M	7	Humerus, shaft	60	Tumor; pain; limitation of motion	.....	Excision, October, 1927	Cancellous bone; adult and calcifying cartilage	Well 4 yr.
22070	W	M	25	Femur, lower, left	240	Tumor	Multiple rounded exostosis	No operation	.....	Well 11 yr.
22005	W	M	25	Os calcis	..	Gonorrheal arthritis	Calcaneal spurs	Excision, August, 1917	Cancellous bone and calcified bone in tendon	Discharged well
21915	W	M	..	Humerus	..	Tumor	.....	Excision, July, 1917	Cancellous bone; adult cartilage	Well over 12 yr.
21680	W	M	34	Os calcis	60	Gonorrheal arthritis	Calcaneal spurs	Excision, June, 1917	Cancellous bone and cartilage in tendon	Recurred, arthritis
21482	W	M	..	Femur, upper	.	Fracture; exhuberant callus	.....	Excision, February, 1917	Cancellous bone; adult cartilage	Discharged well
31424	W	M	..	Fifth lumbar vertebra	..	Pain; tumor	.....	Excision, April, 1917	Cancellous bone; adult cartilage	Discharged well
21208	W	F	15	Femur, lower, left	24	Tumor	Pedicle exostosis	Excision, March, 1917	Cancellous bone; adult cartilage, myxoma	Well 13 yr.
20881	W	M	..	Os calcis	..	Tumor; pain	Calcaneal spurs	Excision, January, 1917	Cancellous bone	Well 2 yr.
20787	W	M	..	Os calcis	..	Pain	Calcaneal spurs	Excision, January, 1917	Cancellous bone; adult cartilage	Dead other causes
20303	W	M	..	Os calcis	..	Pain	Calcaneal spurs	Excision, October, 1916	Cancellous bone; adult cartilage	Discharged well
20182½*	W	F	6	Humerus, right; femur; left; ankle; wrist	60	Tumors	Multiple pedicle exostosis	No operation	.....	Unchanged 6 yr.
20156	W	M	..	Os calcis	4	Pain	Calcaneal spurs	Excision, September, 1916	Cancellous bone; cartilage, myxoma	Well over 13 yr.
18751	W	M	51	Vertebra, ninth dorsal	12	Pain	.....	Excision, 1915; 1916	Cancellous bone; adult cartilage	Dead, second operation
18697	W	M	28	Os calcis	48	Gonorrheal arthritis	Calcaneal spurs	Excision, December, 1915	Cancellous bone	Arthritis recurred 6 yr. later
18585	W	F	..	Skull	..	Tumors	.....	Excision, 1915; 1916	Cancellous bone	Recurred
18505	W	M	33	Fibula, head	1	Tumor	Broad exostosis	Resection, October, 1915	Cancellous bone	Well over 14 yr.
17387	W	M	16	Femur, left	..	Tumor	.....	Excision, April, 1915	.....	7 yr. well
17003	W	F	54	.....	..	Tumor	.....	Excision, February, 1915	Cancellous bone; adult cartilage	No improvement 7 yr.
16695	W	F	27	Femur, lower, right	60	Stiffness; pain	Fracture through pedicle exostosis	Excision, December, 1914	Cancellous bone; adult cartilage	Discharged well
16692	W	M	30	Os calcis	..	Pain	Calcaneal spurs	Excision, December, 1914	Cancellous bone; adult cartilage	8 yr. well
16624	W	M	13	Humerus, left	48	Tumor	.....	Excision, December, 1914	Cancellous bone; adult cartilage	Discharged well
16491	W	M	48	Big toe, right	..	Tumors	.....	Excision, November, 1914	Cancellous bone; adult cartilage	Discharged well
16420	W	M	..	Fibula, upper	..	Tumor after typhoid fever	Broad exostosis	No operation	.....	.....
16286	W	M	..	Femur	84	Tumor; pain	.....	.....	.....	.....
16273	W	M	31	Astragalus	..	Tumor	.....	Excision, September, 1914	Cancellous bone; adult cartilage	Discharged well

TABLE 1.—*Benign Osteochondromas (Exostoses)—Continued*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment
15932	W	M	48	Foot, right	72	Tumor	.....	Excision, June, 1914	.....	Discharged well
15910	W	M	39	Tibia, upper	24	Tumor	.....	Excision, 1914	Adult cartilage; new bone	Well 7 yr.; suicide
15803	W	F	20	Toe	36	Tumor	.....	Excision, May, 1914	Cancellous bone; adult cartilage	6 yr. well
15535	W	M	15	Femur, lower, right	72	Tumor	Broad exostosis	Excision, March, 1914	Cancellous bone; adult cartilage	2 yr. well
15203*	W	M	31	Both feet	144	Pain	.....	Excision, January, 1914	Cancellous bone; adult cartilage	Discharged well
15022	W	M	45	Scapula, right	1	Pain and muscle atrophy	.....	Excision, December, 1913	Cancellous bone in tendon	Well over 16 yr.
14865*	W	M	34	Second and third lumbar vertebra	12	Pain	.....	Excision, November, 1913	.....	Dead
14937	C	F	33	Lower jaw	48	Tumor	.....	Excision, November, 1913	Cancellous bone	Discharged well
14744	W	M	15	Femur, lower, right	60	Tumor; pain	Pedicle exostosis	Excision, October, 1913	Cancellous bone; adult cartilage	Discharged well
14671	W	M	29	Os calcis	14	Trauma; tumor	.....	Excision, September, 1913	Cancellous bone; fetal cartilage	Well 6 yr., lost
14590	W	F	54	Radius, lower, right	3	Pain; tumor	.....	Excision, August, 1913	Cancellous bone	Well 9 yr.
14342	W	M	42	Os calcis	84	Pain	.....	Excision, 1913; 1916	Cancellous bone; cartilage, myxoma	Improved 5 yr. after recurrence
14331	W	M	15	Fibula, lower, left	3	Trauma; tumor; pain	.....	Excision, June, 1913	Cancellous bone; calcifying cartilage	Well 6 yr.
14249*	W	M	15	Fingers, both hands	156	Tumor; pain	.....	Excision, June, 1913	Adult cartilage	Well over 16 yr.
14175	W	M	22	Femur, lower, right	3	Tumor	Pedicle exostosis	Excision, May, 1913	.....	Discharged well
13803	W	M	..	Tibia, lower	24	Tumor	Pedicle exostosis	Excision, 1913	Cancellous bone; adult cartilage	Discharged well
13722	..	..	..	Finger	..	Tumor	.....	Amputation, 1913	Cancellous bone; adult cartilage	Discharged well
13283	W	M	24	Os calcis	18	Pain; tumor	.....	Excision, October, 1912	Cancellous bone; adult cartilage	Discharged well
12770	W	M	22	Humerus, upper, left	180	Tumor	Broad exostosis; cartilaginous cap	No operation	.....	Unchanged
12493*	C	M	9	Humerus and femur	48	Multiple tumors pathologic fracture of femur	Central and periosteal changes in femur	Excision and curettement of humerus	Cartilage; no myxoma	Well 10 yr.
11957	W	F	65	Os calcis	36	Trauma; tumor	.....	Excision, August, 1911	Cancellous bone in tendon	Well 10 yr.; died of other causes
11895	C	F	50	Skull	..	Tumor	.....	Excision, August, 1911	.....	Dead after 4 yr.
11891	W	M	16	Femur, lower	1	Pain	.....	Excision, June, 1911	.....	Well 16 yr.; died of other causes
11354	W	F	28	Femur, lower	192	Trauma; tumor	.....	Excision, February, 1911	.....	Discharged well

11053	W	M	42	Skull	288	Trauma	.....	No operation	.....	Well 11 yr.
10123	W	F	7	Metacarpal	..	Tumor	.....	Excision, November, 1909	Cancellous bone; adult cartilage	Discharged well
9916	W	M	23	Os calcis	48	Pain	.....	Excision, 1909	.....	Discharged well
9890	W	F	27	Femur, lower	180	Tumor	Pedicle exostosis	Excision, August, 1909	.....	Discharged well
9720	W	M	30	Humerus	48	Tumor	.....	Excision, May, 1909	Cancellous bone; adult cartilage	Well 13 yr.
9675	W	M	12	Cervical spine	30	Pain	Rounded exostosis	Excision, May, 1904	New bone; fibrous tissue	Well 25 yr.
9602	W	F	27	Femur, lower	36	Tumor; pain	.....	Excision, March, 1909	.....	Discharged well
9029	C	M	23	Femur, lower	24	Tumor; limitation of motion	Pedicle exostosis	Excision, June, 1908	Cancellous bone; adult cartilage	Discharged well
7881	W	M	24	Femur, lower	8	Trauma; pain; tumor	.....	Excision, January, 1907	Cancellous bone; adult cartilage	Well 23 yr.
6815	W	F	40	Humerus, upper, right	4	Tumor	Pedicle exostosis	Excision, October, 1905	.....	Well 24 yr.
6367	W	M	30	Ilium, crest	6	Tumor	Fuzzy broad exostosis	No operation	.....	Well 12 yr.
6281	C	F	12	Femur, lower, left	36	Tumor; pain	.....	Excision, April, 1905	Cancellous bone	Discharged well
6252	C	M	21	Femur, lower, right	144	Tumor; pain	Rounded exostosis	Excision, May, 1905	Cancellous bone; adult cartilage	Well 16 yr.
6023	W	F	..	Tibia, upper	..	Tumor	.....	.....	.....	.....
5957	C	M	24	Tibia	48	Trauma; ulcer	.....	Excision, December, 1904	.....	Discharged well
5813	W	M	14	Tibia, shaft	36	Tumor; pains	.....	Excision, October, 1904	.....	Dead other causes
5646	W	F	12	Toe, phalanx	..	Tumor	.....	Excision, July, 1904	.....	Discharged well
5488	W	M	24	Tibia, lower	..	Tumor	.....	No operation	.....	Unchanged
5526	W	F	45	Upper jaw	168	Tumor; pain	Rounded exostosis	Excision, May, 1904	Cancellous bone; fibrous tissue	Recurred 9 yr. later
5392	C	M	18	Os calcis	5	Gonorrheal arthritis	Calcaneal spurs	Excision, March, 1904	.....	Discharged well
4412	W	M	52	Femur, shaft	228	Trauma; tumor	.....	Excision, 1902	.....	Well 20 yr.
3822	W	M	11	Scapula, right	48	Tumor	.....	Excision, August, 1901	.....	Well over 28 yr.
3746	W	F	17	Jaw, left, lower	36	Tumor	.....	Excision, 1895	.....	.....
3593	W	F	54	Ischium	120	Pain	.....	Excision, 1895	.....	Well 3 yr. later
2914	W	F	13	Scapula, left	48	Tumor	Pedicle exostosis	Excision, 1900	Cancellous bone; adult cartilage	Discharged well
2497	W	F	15	Sternum	24	Pain	.....	No operation	.....	Unchanged
2071	W	M	51	Tibia, tuberosity	84	Pain	.....	.....	.....	Well 9 yr. later
1652	W	M	22	Big toe	..	Tumor	.....	Excision, 1892	.....	Discharged well
1622*	W	F	10	Radius	1	Multiple tumors	.....	Excision, 1892	.....	.....
1257	W	F	25	Femur, lower	168	Tumor; pain	Pedicle exostosis	Excision, 1891	.....	.....
7521	W	M	45	Scapula	60	Tumor	.....	.....	.....	.....
800	W	M	30	Humerus, upper	18	Pain; tumor	.....	Amputation, 1894	.....	Dead other causes 7 yr. later
743	C	F	41	Skull, frontal	98	Trauma; tumor	.....	Excision, 1890	.....	.....
739	W	M	20	Jaw, lower angle	36	Tumor	.....	Excision, 1890	.....	Well 8 yr. later
590	W	M	33	Femur, lower	5	Trauma; tumor	.....	Excision, 1891	.....	.....
502	W	F	11	Tibia, head	6	Tumor; pain	.....	Excision, June, 1890	.....	Well 32 yr.
440	C	F	18	Scapula	448	Tumor	.....	Excision, 1890	.....	.....

duration of symptoms corresponds closely to the average time of four and one-half years computed by Meyerding [4] in a study of 232 cases reported from the Mayo Clinic. This protracted course bespeaks benignity, for in this condition, as in most neoplasms, the longer the duration of symptoms the greater the curability of the disease.

The benign course of these lesions is further reflected in the character of the symptomatology. Pain is rarely severe, and when other than a mild ache or discomfort is present there is usually some complicating factor. Such complicating factors may take the form of bursitis or infection from irritation in the overlying soft parts, or repeated trauma may bring on such a condition in a region where swelling interferes with the use of the affected member.

More rarely, acute symptoms may follow a sudden increase in the rate of growth in the tumor. Compression of important vessels may cause edema and pain and bring the patient under observation. When such acute symptoms can be attributed to an increased growth rate in the tumor, malignant change is always to be suspected. It is a common and justifiable habit of clinicians to be influenced in favor of making the diagnosis of a benign condition when the history of the tumor extends over a number of years, as it does in most cases of exostoses. It is therefore important to call attention here to the fact that despite the duration of the disease, malignant change marked by exacerbation in the symptomatology may take place at any time in these lesions, and in such cases the most important evidence is the growth rate in the tumor and not the duration of the disease. In making a diagnosis of malignancy, it is helpful to know that the malignant change is most frequent after the age of 30 and that care must be taken to rule out an acute bursitis or inflammation in the overlying soft parts.

The location of the lesion is an important factor in leading to its discovery, although tumors in any area may be accidentally disclosed by a roentgenographic examination made for other reasons. Exostoses occurring about the pelvis are particularly prone to exist without giving any clues to their presence.

Stiffness in the adjacent joint after prolonged use of the limb is not an infrequent symptom. Apparently the stiffness or limping is brought on through irritation by the bony tumor to the overlying ligaments and tendons during the use of the limb. Rest of the affected part brings early relief from these symptoms.

Physical examination of the patient with exostosis is usually productive of only local observations. In only two instances in this series was there a positive Wassermann reaction or definite syphilitic history, and the blood and urine were uniformly negative. In a definite percentage

4. Meyerding, H. W.: Exostosis, Radiology **8**:282 (April) 1927.

of the cases in which some systemic or hereditary factor is operative the lesions may be multiple. Arthritis associated with gonorrheal infection may be a determining factor in such instances.[5] A familial disease known as hereditary deforming chondrodysplasia may be responsible. This last group of hereditary multiple exostoses is discussed subsequently.

Local examination of the tumor reveals a firm swelling securely attached to the underlying bone. There is little or no tenderness to be

Fig. 4 (P. N. 35720).—Roentgenogram showing a typical exostosis in the upper end of the tibia near the insertion of the quadriceps tendon. The outgrowth is continuous with the normal bone beneath and a distinct bursa overlies the exostosis. The presence of a calcareous bursitis makes this complication clearly visible.

made out on deep pressure. The soft parts overlying the tumor are most often freely movable unless there has been undue irritation with

5. While the osteophytes common to hypertrophic arthritis are not included in this study, selected cases of calcaneal spurs in gonorrheal arthritis (in which the microscopic changes were indistinguishable from osteochondromas) have been included to emphasize the point that the tissue of origin, and not the etiologic agent is the determining factor in all of these neoplasms.

inflammation. At times the mass will feel much larger than might be expected from its size in the x-ray film. If the bulk of this mass is firm and rubbery, a large proportion of cartilaginous tissue that is invisible in the roentgenogram will be found. If fluctuation is obtained, an overlying bursa containing fluid may be responsible, this bursa being occasionally visualized in the roentgenogram (fig. 4) when there are calcareous deposits in the synovial fluid of the sac.

Fig. 5 (P. N. 39602).—Exostosis of the pedicle type at the site of the adductor tubercle in the lower end of the femur. Note the widened metaphyseal region near the outgrowth and the extension of the pedicle in the direction of the pull of the adductor magnus muscle. The osseous portion of the outgrowth is continuous with the underlying normal bone, and the neoplastic cartilaginous cap is well outlined by calcification.

ROENTGENOGRAPHIC FEATURES

The roentgenographic appearance of an exostosis is determined by its mode of attachment to the underlying bone and the size and character of its overlying cartilaginous cap. If the attachment to the underlying bone is by means of a tapering pedicle, the exostosis is usually

referred to as the pedicle type (fig. 5). If the attachment to the bone is represented by a broad area which merges imperceptibly into the shaft of the bone, the exostosis is generally referred to as the broad base type (fig. 6). Occasionally, the exostosis may be attached to the underlying bone by an extremely narrow pedicle, or one which has become fractured and resorbed so that no apparent bony connection is visible in the roentgenogram. This however, is the exception.

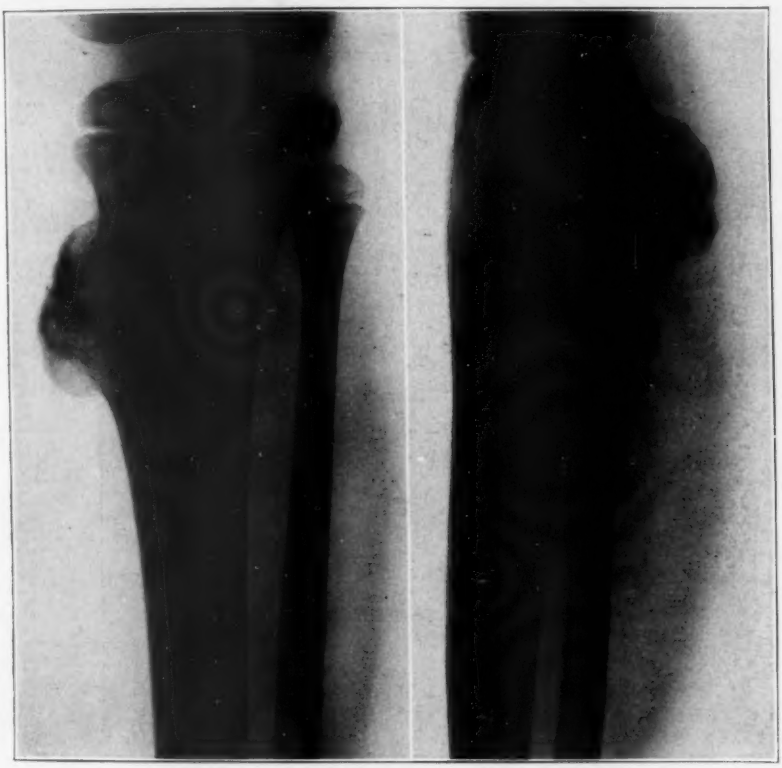

Fig. 6 (P. N. 42142).—The roentgenographic appearance of the broad base type of exostosis. In this case there is a bulging of normal bone over a wide area at what is normally the site of the tibial tuberosity. There is little calcification in the thin overlying cartilaginous cap.

The structure of the pedicle or base of the exostosis is one of its characteristic roentgenographic features. This bony attachment is composed of bone differentiated into cancellous and cortical zones, and these zones are both merged imperceptibly with the normal cortical and medullary portions of the bone beneath. There is much histologic evidence to indicate that the entire pedicle or base of the exostosis is not of true tumor origin but represents an outpouring of normal osseous

tissue through a gap in the overlying periosteum. The most important feature therefore in the roentgenographic appearance of the exostosis when differentiating it from sarcoma is not the bony attachment but the neoplastic cartilaginous cap.

This cartilaginous cap of the exostosis may vary from a small, nearly invisible overlying zone (fig. 6) to a large calcifying cauliflower mass (fig. 7). If this cartilaginous mass is small or if it is definitely or faintly outlined with calcified material, there need be no hesitancy in making the diagnosis of a benign lesion. When, however, the car-

Fig. 7 (P. N. 39064).—Osteochondroma at the lesser trochanter of the upper end of the femur in which the neoplastic cartilaginous cap predominates in the form of a calcifying cauliflower mass. Although this growth bulges into the soft parts in many directions, the absence of bone destruction in the underlying tuberosity and in the base of the exostosis indicates a benign lesion. This picture should be compared to figure 8.

tilaginous mass is large and ill defined on its outward margin and when its calcified areas are being resorbed and present a granular appearance and when, in addition, these more translucent zones are secondarily invading the bony base or pedicle, malignancy is to be suspected, and the symptomatology is to be carefully checked (fig. 8).

In addition to the roentgenographic appearance of the exostosis itself, it is always useful to examine the adjacent metaphyseal region of

the involved bone. A wide metaphyseal zone as pointed out by Jansen [6] is typical of fully developed or mild degrees of hereditary chondrodysplasia, a diffuse disease of the skeleton with which benign, single or multiple exostoses are often associated.

Exostoses occurring on the shaft side of the long bones, particularly in the region of the thigh or elbow, must be differentiated in the roentgenogram from myositis ossificans traumatica. In ossifying myositis, the ossifying mass has often no attachment to, and is not continuous

Fig. 8 (P. N. 37868).—Osteochondroma at the greater trochanter of the upper end of the femur which has undergone secondary malignant change. Note the granular and hazy outward margin of the calcified cartilaginous cap and the bone destruction mottling the area of the femur just below the trochanters. The patient was a white man, aged 29, who died eight years after the first symptoms with metastases. The roentgenogram was taken three months before death. Compare with figure 7.

with, the underlying bone. It presents a typical parallel laminated appearance and lacks the characteristic cartilaginous cap so often seen

6. Jansen, M.: Dissociation of Bone Growth (Exostoses and Enchondromata) or Ollier's Dyschondroplasia and Associated Phenomena, The Robert Jones Birthday Volume, 43-72, Oxford University Press, London, 1928.

in benign exostosis (fig. 9). The definite history of trauma followed in about six weeks by a hard mass of stationary size typical of myositis ossificans traumatica is an important clinical distinction.

GROSS PATHOLOGY

At operation or after excision, an exostosis has the appearance of a firm lobulated tumor overlaid by a smooth and glistening fibrous surface (fig. 10). If the tumor is cut into, the shiny surface is readily seen

Fig. 9 (P. N. 36014).—Roentgenogram in a case of myositis ossificans traumatica. The ossifying mass is separated from the shaft of the underlying bone at the upper and lower portions by a slight interval. There is a definite outward margin to the growth and the densest part of the shadow is streaked in a direction parallel to the underlying shaft. This growth subsequently became malignant and the patient died with metastases.

to be composed of two layers, one a thin fibrous envelop not exceeding 1 mm. in thickness, and the other a translucent cartilaginous zone, generally less than 1 cm. in thickness. Beneath these two layers the bulk of the tumor mass, which is composed of cancellous bone, is found. The relative proportions of cartilage and bone in the usual exostosis is

subject to variation. While it is true that the cartilage composes only a thin cap in most of the tumors, still in other growths this more primitive type of tissue may constitute so much of the bulk that these tumors have been described as periosteal chondromas. The greater the percentage of cartilage in the tumor, the more frequently it is composed of knotty masses or definite lobules (fig. 11).

The relationship of the muscular attachments entering the tumor areas are most significant. The tendon ends are often blended imper-

Fig. 10 (P. N. 40040).—Outward appearance and sectioned surface of an excised exostosis. On the outward surface is seen the glistening membrane to which fibers of the tendon have been attached at nodular points. On the cut surface, the thickness of the cartilaginous portion overlying the cancellous bone is plainly visible.

ceptibly with the thin fibrous membrane which overlays the cartilaginous cap. Even under the microscope, this merging of the tendon with the tumor capsule can be seen (fig. 12), and on this relationship hinges largely the conception of the histogenesis of these tumors.

Since under the microscope these growths can be shown to be arising from strands of fibrous tissue, it becomes exceedingly important to

determine the source of this connective tissue and to know whether it springs from tendon, periosteum or aberrant islands of the joint capsule. In the present study, specimens removed at operation were dissected and sections cut from the various margins or zones to determine this relationship of connective tissue to the tumor proper. Two types of fibrous tissue were found in the capsule of the growth. The first was intimately associated with the cartilaginous portions of the tumor, but outwardly infiltrated into the soft parts to become lost in the tendons of the adjacent muscles. The other was also associated with cartilage formation, but its margin extended along the normal bone and merged into the periosteum. In other words, the cartilaginous portion of the tumor seemed to be united by connective tissue to bone on the

Fig. 11 (P. N. 26392).—Gross specimen showing the nodular and lobulated cartilaginous portions in an exostosis in the upper end of a fibula in a white girl, aged 14. A cure was effected by resection.

one hand and to the tendon ends on the other. From this analysis, it was logical to conclude that these exostoses represented an abnormality in a tissue of union interposed between tendon and bone. Under normal circumstances, this tissue of union is most often a bony protuberance or tubercle provided for the attachment or insertion of an important muscle.

Notwithstanding this interpretation, the way in which the cartilaginous and membranous tissues overlay the bony portion of the osteochondroma in the gross specimen suggests strongly that these tumors represent an abnormal articulating surface of bone. The lobulated contours of the external surface of the tumor are covered by a smooth, glistening layer of cartilage which is analogous to the normal joint

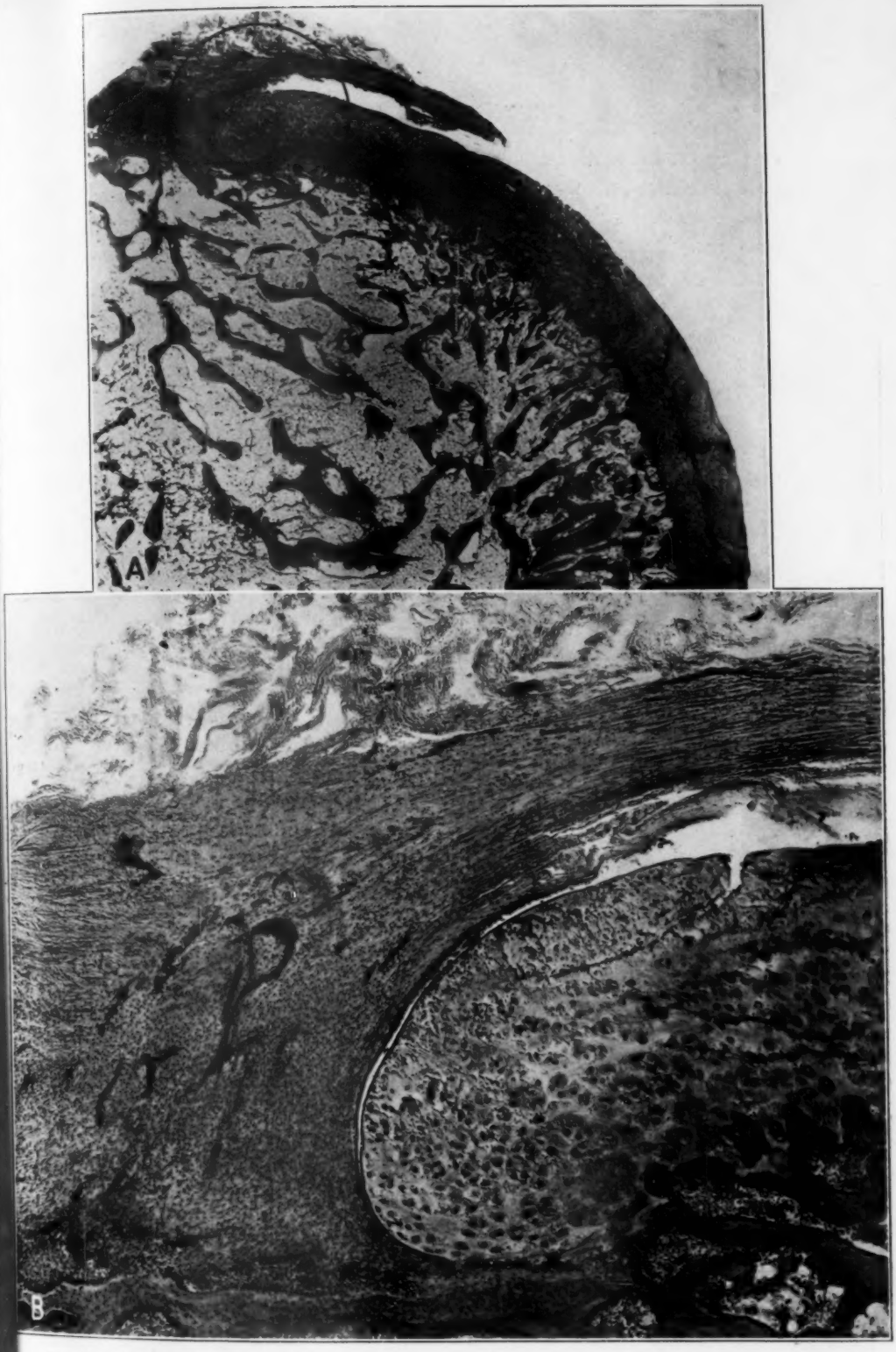

Fig. 12.—Microscopic studies showing the relationship of a benign exostosis to an adjacent tendon. *A* shows a low magnification of an exostosis with a piece of overlying tendon partially encircling the cartilaginous cap. The tendon is seen in the upper left hand corner, and beneath the cartilaginous rim is a large area of cancellous bone enclosing fatty bone-marrow. *B* shows a higher magnification taken from the area marked in *A*. The cellular primitive connective tissue embedded in the tendon is giving rise to cartilage on the one hand and to membranous bone on the other.

cartilage at the end of a long bone, and this outward layer of chondral substance is in turn surmounted by a thin transparent fibrous membrane which duplicates in many respects the perichondrium overlaying the normal articular cartilage (fig. 13). The core of the tumor is com-

Fig. 13 (P. N. 28770).—Low power photomicrograph of the normal articular surface of the lower radius. The picture shows the joint cartilage, the zone of provisional calcification and the underlying normal bone. Most of the perichondrium overlying the cartilaginous surface was lost in making the preparation. Note how the transition from cartilage to bone follows the order shown in the exostosis in figure 15.

Fig. 14 (P. N. 28770).—Higher magnification of area marked in figure 13 at the point of reflexion of the joint capsule. At this point there persists primitive precartilaginous tissue giving rise to cartilage. This is a normal growth center.

posed of cortical and cancellous bone which for all practical purposes is identical with normal osseous material at the articular ends of bone. To emphasize further this analogy, at operation an overlying bursa is not rarely encountered over the exostosis, which simulates the bursae associated with normal joints.

This composite interpretation of the gross specimens of osteochondromas, relating them on the one hand to exaggerated normal bony

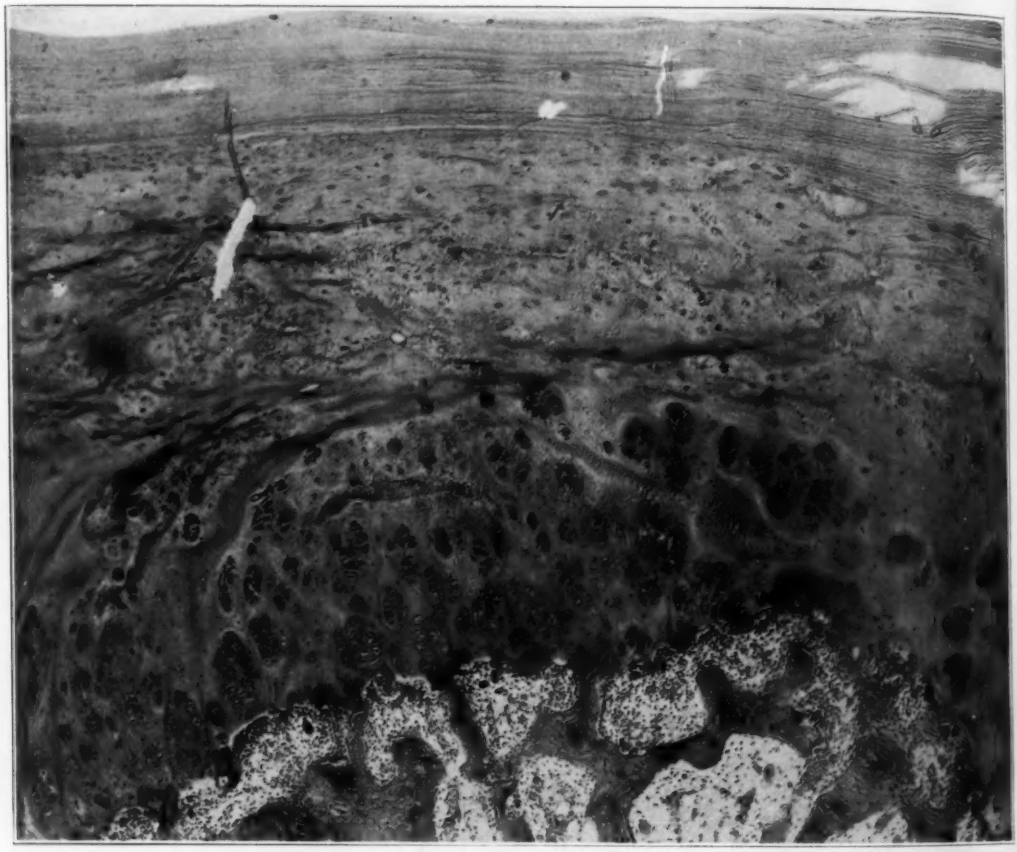

Fig. 15 (P. N. 26392).—Photomicrograph from the specimen shown in figure 11. The overlying membranous portion of the exostosis shows in the upper right hand corner the direct continuation of fibers of an adjoining tendon. The entire histogenesis of the neoplasm can be traced in this picture. At the upper margin is the primitive connective tissue which is the mother substance of the tumor. This tissue is giving rise to a small amount of fetal cartilage, beneath which there is much typical normal adult cartilage, calcifying in its deeper layers. Beneath this, there is a protusion of normal adult bone enclosing a small amount of fatty marrow.

protuberances, and on the other to supernumerary articular surfaces, is justifiable on the basis of their histology as well as their gross pathology. For histologically, these tumors are derivatives of a primitive periarticular tissue which normally serves such multiple functions.

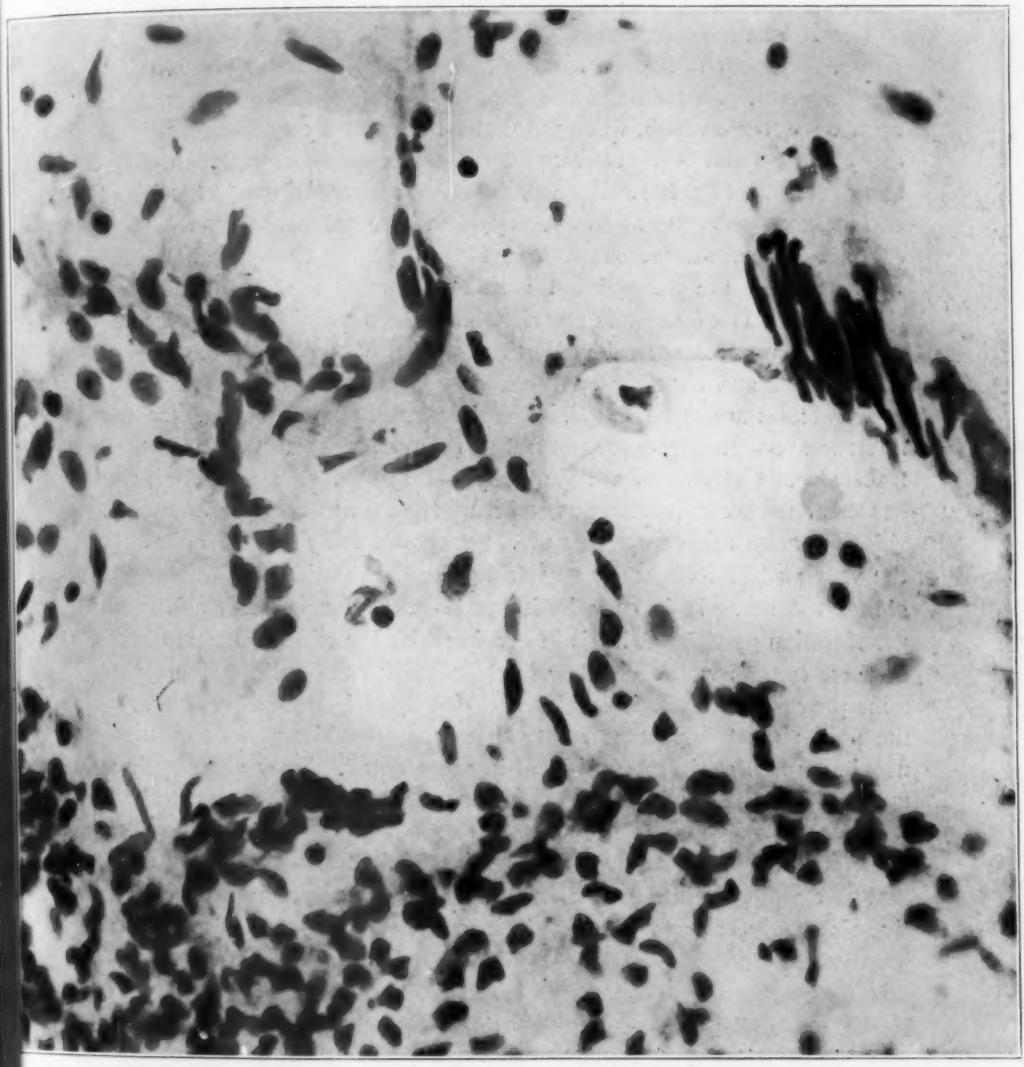

Fig. 16 (P. N. 41267).—High power photomicrograph of a cellular area at the membranous margin of an exostosis. The dense cluster of spindle cells near the upper right hand corner are embryonic connective tissue cells. The clear space beneath is the hyaline substance of myxoma and the three cells with the dense nuclei are fetal cartilage cells. This illustrates the transition from connective tissue to cartilage (the myxoma phase) which is the neoplastic process in osteochondroma and in all tumors of the fibrocartilaginous group.

MICROSCOPIC FEATURES

The typical microscopic picture of the osteochondroma seen under low magnification is shown in figure 15. The tumor, passing from the superficial layers to the deeper ones adjacent to the normal underlying bone, shows a characteristic transition from fibrous tissue to cartilage to bone. The most superficial layer is generally a hyalinized connective tissue, very poor in nuclear material, which caps the tumor over its outward surface. At points in this cap, there are islands of more cellular connective tissue which, when put under high power magnification, show many small spindle-shaped nuclei arranged in syncytial fashion, resembling myxoma (fig. 16). Beneath the fibrous layer is found a hyalinized cartilaginous substance. In the regions where the connective tissue is cellular, there are numerous fetal cartilage cells, but these small areas of fetal cartilage are insignificant beside the major portion of chondral tissue which is of the adult variety and resembles in all respects the typical chondroma. In its deeper portions this cartilage undergoes calcification, and abutting on the zone of calcified cartilage laminated bony spicules are to be found. This laminated adult bone is cancellous in structure with a generous amount of fatty bone-marrow between its trabeculae. Osteoblasts are generally not applied to the spicules, nor has this bone the coarse fibrous structure typical of new bone formation.

The entire microscopic picture is preponderantly one of quiesence, the varying histologic zones appearing like the stratified deposits of an obliterated sea. It is only in isolated zones that evidence of active proliferation persists. This is in keeping with the clinical characteristics of these tumors which are slow in their growth and mild in the symptoms provoked. These isolated areas of cell proliferation, however, are the points most important for the study of the histogenesis of these neoplasms and must be considered in more detail. They also supply a nucleus for the malignant change that occasionally occurs in these tumors.

In the areas of cellular fibrous tissue, the capsule dips into the tumor, dividing it into lobules. These penetrating strands of connective tissue give rise to groups of fetal cartilage cells and also in rare instances to small amounts of new bone. It is therefore plainly evident that the mother substance of the cartilaginous portion of these tumors is the precartilaginous connective tissue found indenting the tumor from its periphery. Although this early connective tissue must also be ascribed the function of new bone formation, it is by no means certain that the large amount of adult bone comprising the bulk of the exostosis is derived from this same mother substance. The entire mass of this adult bone is so intimately related with the shaft of the underlying normal bone that it appears to be arising as a protrusion of the shaft, rather than as a deposit of the small amounts of osteogenic tissue

found in the neoplastic portions of the cartilaginous cap. If this interpretation is correct in the histogenesis of these tumors, it becomes necessary to explain not only the origin of the cartilaginous growths that form the cap of the exostosis, but also to account for the independent proliferation of normal bone beneath which constitutes the pedicle or base of the osteochondroma.

HISTOGENESIS

The close simulation of the usual exostosis to a normal articulating surface of bone, as well as the relationship that the location of the tumor

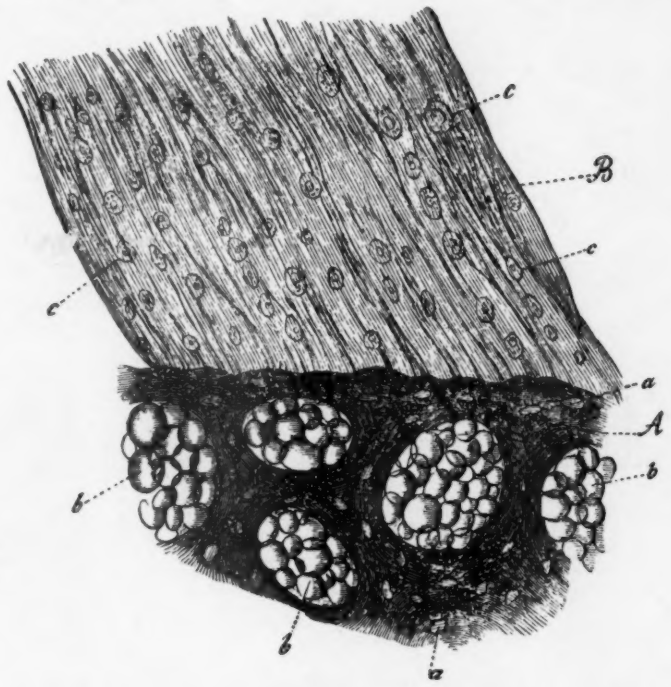

Fig. 17.—This drawing reproduced from Kollicker depicts cartilage cells (*c*) in the end of the achilles' tendon (*B*) which attaches directly to the bone of the os calcis (*A*). This is the first known record of the discovery of precartilaginous connective tissue giving rise to cartilage in the substance of a tendon. (After Kollicker: Human Histology, London, Sydenham Society, 1853, vol. 1, p. 251.

generally has to points of tendinous attachments, focus attention on the embryology of these normal structures. In both normal tendons, which attach directly to bone, and in normal joints at the reflexion of the joint capsule, proliferating zones apparently acting as normal growth centers may be found. In these proliferating centers early cartilage cells derived from young fibroblasts may be seen (figs. 13 and 14), and occasional areas of ossification, a transition of tissues typical of

Fig. 17A (P. N. 48035).—Low power photomicrograph showing the attachment of the extensor carpi radialis longus to the metacarpal in a white man, aged 31 (the hand was amputated for a sarcoma of the soft parts occurring in another portion of the hand). The illustration shows the persistence of precartilaginous connective tissue with the proliferation of cartilage, forming a junction between the bone in the upper portion of the picture and the tendon in the lower. This embryonic tissue of union between tendon and bone, which can be observed microscopically under normal conditions at the sites where chondromyxosarcomas arise, refutes the current misconception in regard to the origin of such tumors by a process of dedifferentiation.

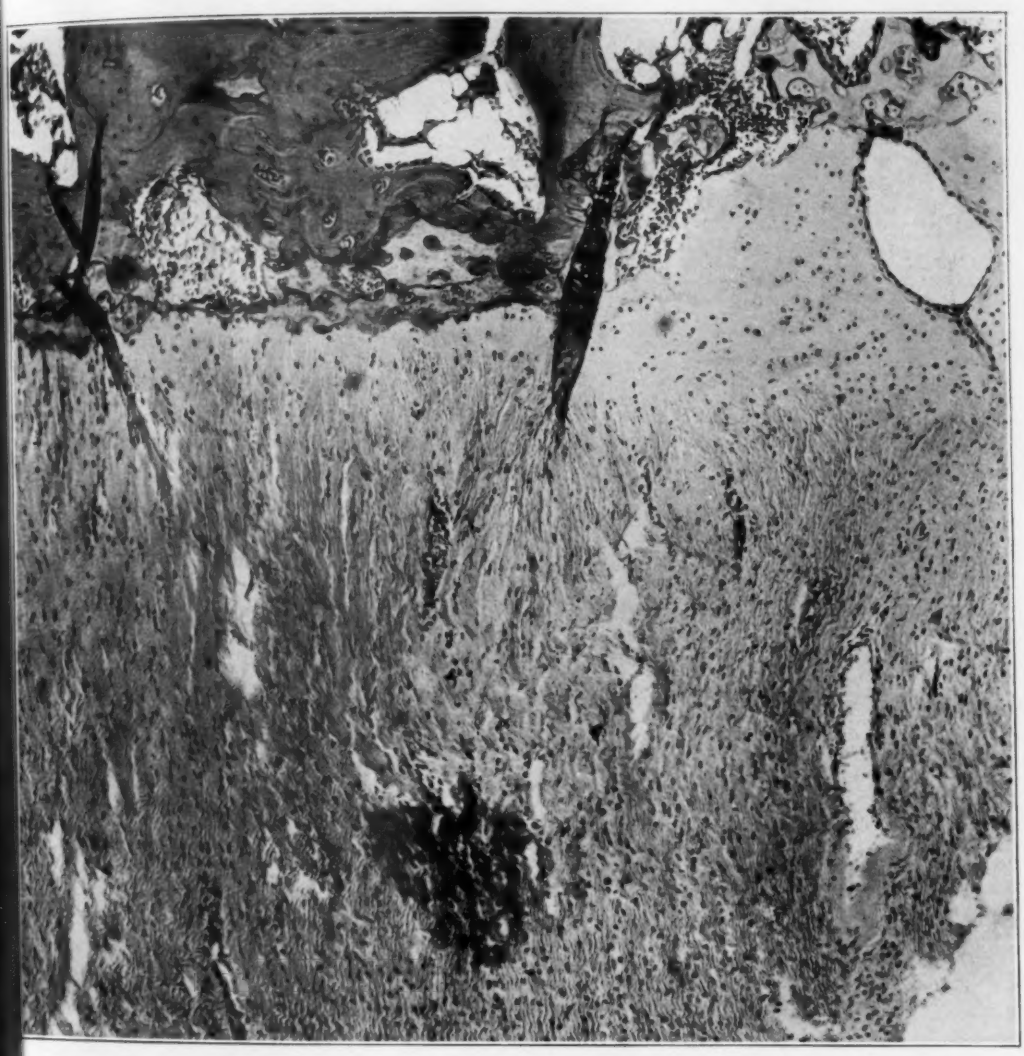

Fig. 17B.—Low power photomicrograph showing precartilaginous connective tissue with cartilage formation at the insertion of the quadriceps tendon into the tibial tuberosity in a young dog. This photograph should be compared with figure 17A. The embryonic tissue of union shown in this picture persists in practically an identical form even in later life as shown in figure 17A.

Fig. 18.—Osteogenic processes in tenosynovitis associated with calcareous bursitis. In the lower right hand corner is seen dense embryonic fibrous tissue which is proliferating cartilage that is undergoing calcification and ossification. (After Harbin: Arch. Surg. **18**:1510 [April] 1929).

the osteochondromas. The occurrence of such proliferating zones in normal tendon ends was first observed by Kollicker [7] in 1853 (fig. 17) and similar transitional zones are typical of tenosynovitis associated with calcareous bursitis (Harbin,[8] fig. 18). In the development of joint mice, the studies of Henderson and Jones [9] demonstrated that loose cartilaginous bodies may undergo ossification in the synovial membrane (fig. 19), showing again the relationship of the histologic transitions typical of exostosis to articular and periarticular structures.

Since in normal bones the growth centers at the epiphyseal line contain neither proliferating fibrous tissue nor fetal cartilage cells but

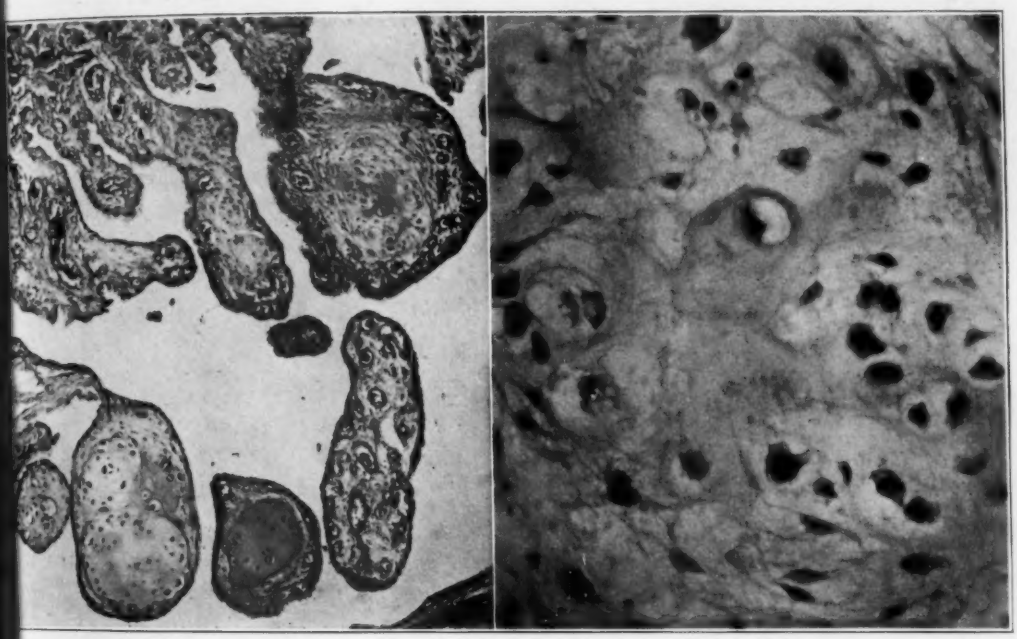

Fig. 19.—Low and high power photomicrographs showing the development of cartilage with subsequent ossification in tags of synovial tissue within the joint cavity. This illustrates the histogenesis of the so-called joint mice occurring in osteochondromatosis of the knee joint and proves the power of cartilage formation residing in the primitive connective tissue of the synovial membranes. (After H. T. Jones: J. Bone & Joint Surg. **6**:407, 1924.)

7. Kollicker, A.: Manual of Human Histology, London, Sydenham Society, 1853-1854, vol. 1, p. 251.

8. Harbin, R. M.: Deposition of Calcium Salts in the Tendon of the Supraspinatus Muscle, Arch. Surg. **18**:1491 (April) 1929.

9. Jones, H. T.: Loose Body Formation in Synovial Osteochondromatosis, with Special Reference to Etiology and Pathology, J. Bone & Joint Surg. **6**:407, 458 (April) 1924.

derivatives in a higher state of differentiation, it is evident that the osteochondromas are not related histogenetically to the bone proper nor to the epiphyseal line as so often stated, but rather to such articular and periarticular structures already cited. This deduction is confirmed by a comparative study of the embryology of the joints, periarticular structures and bone.

Both the bones and joints begin their differentiation from a single type of mesenchymal derivative. This mesenchymal derivative is a simple condensation of embryonic connective tissue which forms at the site of the future skeleton (fig. 20). It represents the precartilagin-

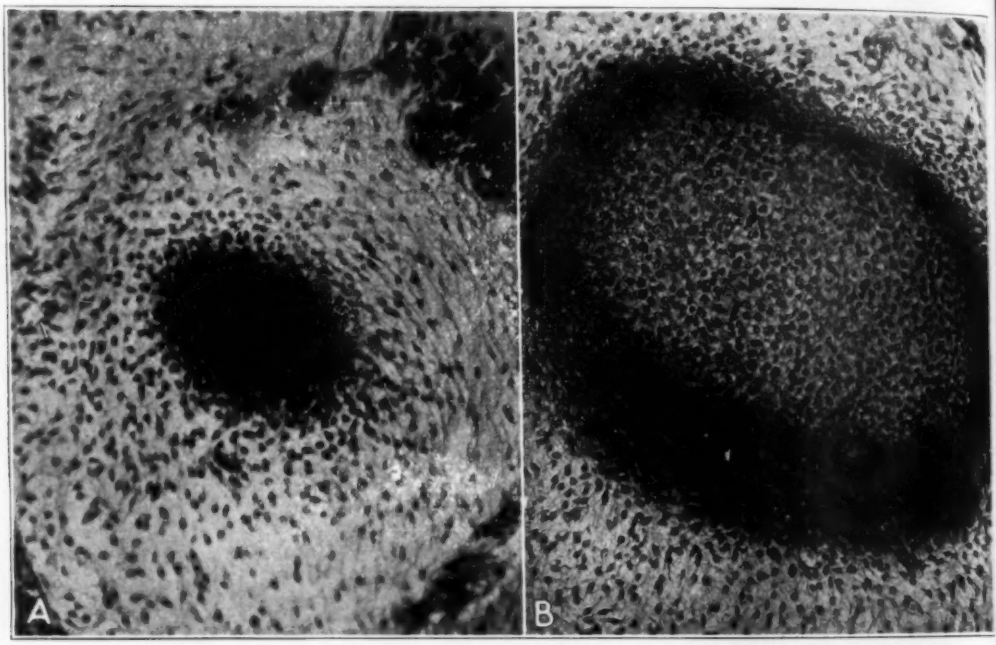

Fig. 20.—Embryo. *A* shows the condensation of embryonic connective tissue (blastema) at the site of the future skeleton, and in *B* this precartilaginous condensation of connective tissue is giving rise at its center to early cartilage cells. The persisting rim of dense connective tissue about the early cartilage cells is the primitive perichondrium and has the power of forming both bone and cartilage. Persisting strands identical in nature with the perichondrium are referred to as precartilaginous connective tissue throughout this paper. The sections were taken from a human embryo 14 cm. in length.

ous state of the future skeleton and is known as blastema. Whereas the blastema of the future skeleton differentiates rapidly into cartilage so as to form an entire cartilaginous skeleton (with exception of the membranous bones) at an early date in embryonic life, the so-called extraskeletal blastema, which is destined to form joints, and the attachments of certain tendons and ligaments lags behind and goes through a

somewhat different cycle of changes. By mucoid regression in this extraskeletal blastema, the joint cavities and certain bursae are formed, and this same embryonic fibrous tissue overlays the joint ends of the bone with the perichondrium from which the joint cartilage is formed on the underlying bone. Where this thick connective tissue coat overlaps and extends beyond the bone, the joint capsule, the ends of ligaments and tendons and the synovia are differentiated.

Thus the joint cartilage, the joint capsule, the synovia, the ends of various ligaments and tendons and the joint cavity as well as associated bursae are all derived from this one mother substance. This extraskeletal blastema tissue in all of its derivatives retains at points the power of cartilage and bone formation throughout life. But unlike the skeletal cartilage differentiated from this blastema at an earlier stage, this type of chondral tissue does not undergo active resorption by giant cells in its calcified state, but becomes converted more directly into permanent bone.

Thus on embryologic grounds, as well as by site and localization, the osteochondromas, because of the histologic cycle from fibrous tissue to cartilage to bone which they show in their growth zones or cartilaginous caps, must be histogenetically related to the extraskeletal blastema or the forerunner of articular and periarticular structures.

In tendons such as the achilles, the quadriceps at its attachment below the knee and the adductor magnus fastening above the medial condyle of the femur union is established not with the periosteum, but directly to bone. These tendons have their osseous ends formed, not by ordinary fibrous tissues, but by extraskeletal blastema (fig. 21), and since the periosteum is normally lacking or deficient at such points, the underlying bone lacks a limiting membrane and grows out in the form of a normal bony protuberance to meet the tendon.[10] Such outgrowths of bone are normal occurrences and are known as the adductor tubicle, the tibial tuberosity, etc. The entire tuberosity, which provides for such ligamentous attachment, however, is not derived from the underlying bone but is added to more indirectly from preceding cartilage formed from the blastema in the ligament or tendon. Both the shaft of the bone and the end of the tendon thus cooperate in the formation of the tuberosity.

Therefore, the normal events at the site of a future exostosis, which must be superseded in order for tumor formation to take place, are: (1) the end of a tendon or ligament formed from blastemal

10. Macewen (The Growth of Bone: Observations on Osteogenesis. An Experimental Inquiry into the Development and Reproduction of Diaphyseal Bone, Glasgow, James Maclehose & Son, 1912) has experimentally shown the power of the periosteum to act thus as a limiting membrane to bone growth.

tissue and destined to aid in the formation of its own bony attachment; (2) an underlying zone of normal bone without periosteal covering destined to form an outgrowth or attachment point in the skeleton; (3) a margin of periosteum surrounding the zone which eventually is to form a sleeve or cuff about this zone.

Fig. 21.—Low magnification of a longitudinal section of the lower leg of the embryo shown in figure 20. The future skeleton is preformed in cartilage. The entire tibia is shown, the cartilage of which is undergoing calcification in the pinched, midshaft region. At *A* is seen the insertion of the quadriceps tendon (embedding the patella) into the future tuberosity of the tibia. The dense black connective tissue of the tendon is persisting precartilaginous connective tissue shown under higher magnification in figure 20. At *B* is seen the dense primitive connective tissue in the region of the insertion of the achilles' tendon. Note the persistence of this dense connective tissue within the future knee joint.

The origin of an osteochondroma or exostosis at such transitional zones depends on abnormal variations in some one of the foregoing factors. If both the zone of cartilage in the tendon end and the bony outgrowth of the underlying bone are normally balanced and eventually overlaid by periosteum, an osteochondroma will not form. If, however, the periosteum surmounts only the outgrowth of the underlying bone and fails to blend with the fibrous tissue of the tendon, the growth of the cartilaginous center in the fibrous attachment of the muscle will not be properly limited, and a tumor results. In such an event, the cartilaginous zone in the tendon overgrows the protuberance of normal bone, overlapping the periosteum and forming a typical exostosis.

It is clear from the foregoing facts that osteochondromas are compound growths, since the underlying osseous pedicle is composed of normal bone which has a deficiency in its periosteal covering, while the overlying cartilaginous cap arises independently from precartilaginous connective tissue in the end of a tendon or ligament.

ETIOLOGY

From a consideration of the histogenesis involved in tumors of the osteochondroma group, the multiplicity of possible etiologic factors becomes apparent. In congenital exostosis, in which these tumors are frequently multiple and often hereditary, there is undoubtedly a tendency to variation in the periosteal apertures about the zones where bony protuberances normally arise. That this congenital variation affects the periosteum and underlying cortical bone primarily as well as the cartilaginous zone of growth in the ligaments and tendons is evidenced by the diffuse metaphyseal widening so often seen in this form of so-called hereditary, deforming chondrodysplasia. Apparently the rim about the periosteal deficiency is either unusually wide or abnormally inactive or both, permitting the underlying bone to protrude in an unusual manner.

In regard to the exostosis of inflammatory origin, such as the calcaneal spurs in gonorrheal arthritis, the fault in this instance is not a deficiency in the activity of the adjacent periosteal cuff but rather an overstimulation of the cartilaginous center in the tendon where the infection has directly initiated an increased growth activity. Likewise, in the osteophytes of chronic arthritis, there is a stimulation of the normal zones of cartilaginous growth which persist near the point of reflexion of the joint capsule and synovial membrane. Despite the unorthodox procedure of classifying these infectious osteophytes with the neoplasms of the osteochondroma group, microscopic distinction between the

two is impossible, and histogenetically, as has just been shown, there is a common basis of origin (fig. 22).

Single exostoses may arise as a result of traumatism to a normal cartilaginous growth zone or where aberrant islands of cartilage with strands of blastemal tissue have been left behind to form embryonic cell rests in the sense of Cohnheim. When traumatism plays an etiologic

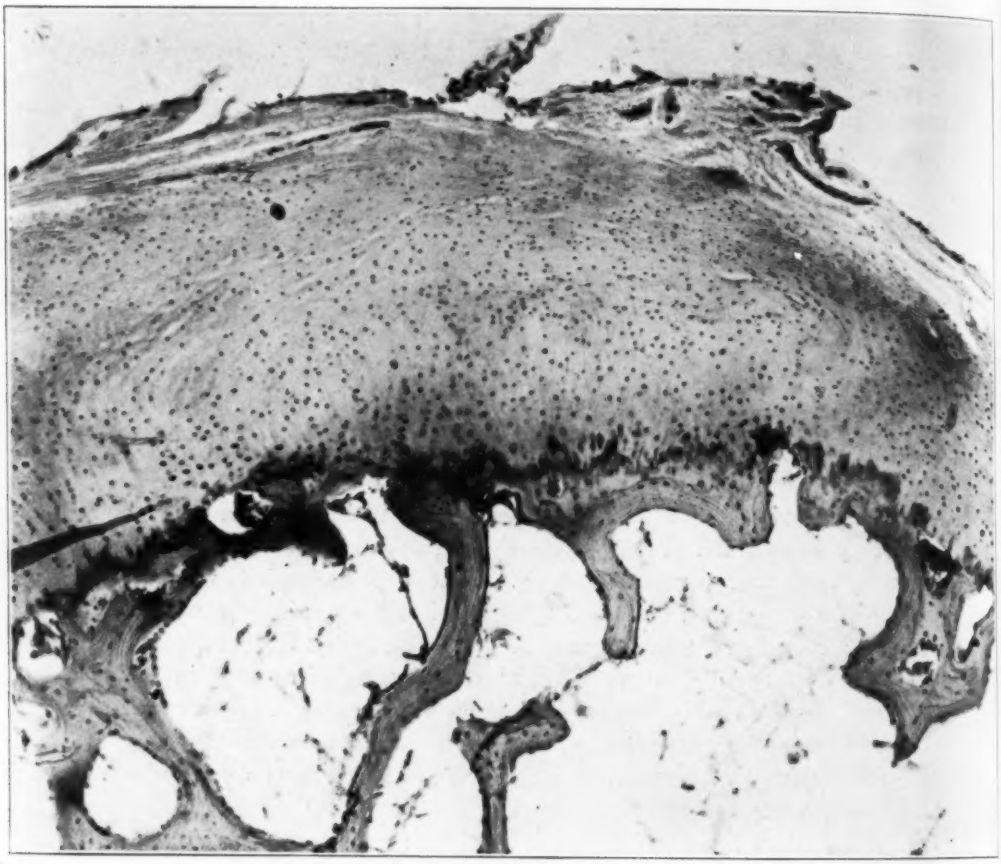

Fig. 22 (P. N. 34167).—Low power photomicrograph of a calcaneal spur in a white man, aged 39, giving a history of gonorrhea thirteen years previously followed by polyarthritis for a number of years, which at first affected all the joints but which finally localized at both ankles. In the picture there is seen the overlying connective tissue continuous with the tendon, the zone of cartilage and the underlying bone typical of all exostoses. Compare this with figure 15.

rôle, it is difficult to determine whether the traumatism is active in repressing the adjacent periosteum or in stimulating the adjacent zone of cartilaginous growth. Conceivably, the injury may result in both, but the latter is more probable. At any event, the trauma probably

functions in disturbing the balance between the permanent bone formation in the underlying osteogenic zones of the periosteum and the proliferating powers in the adjacent precartilaginous tissue.

TREATMENT AND PROGNOSIS

The foregoing analysis of the histogenesis and etiology of exostoses has an important bearing on the treatment and prognosis of the disease. Ordinarily these lesions are benign and represent merely an imbalance between two normal phases of growth in the same manner, as was pointed out in a previous paper in regard to bone cysts and giant cell tumor (Geschickter and Copeland [11]). Operative intervention is frequently not called for, since in the usual exostosis the periosteum and underlying cortical bone succeed eventually in "hemming in" the cartilaginous cap except at the point where the fibrous portions of the tendon or ligament perform an identical function. However, even when such normal balance is restored, operative removal may become necessary because of the interference by the tumor with the function of the surrounding muscles in the use of the adjacent joint. When the location of the tumor is such that repeated injuries result in the formation of a bursitis, the consequent painful lesion warrants operative removal.

In the removal of such an exostosis, a more careful dissection is warranted than is usually given such tumors. The zone of periosteum overlying the adjacent normal bone about the pedicle or base should be carefully delimited and marked out by the knife and laid back. The base or pedicle should then be chiseled through and the tumor lifted off the underlying bone while it is still attached to strands of the adjacent tendon. The fibers of the tendon entering the tumor zone should then be partially dissected and clipped above the cartilaginous zones which are frequently embedded in them. After the growth has thus been removed, care should be taken to provide for the reanchoring of the strands of the tendon and to suture the adjacent fascia and muscles over the rift in the periosteum to aid in the restoration of the normal cortex when healing occurs.

Ordinarily, the usual exostosis, when operated on, is accorded no such systematic treatment. The tumor is chiseled away piecemeal in a careless fashion, the surgeon neglecting the relationship of the adjacent tendons to the tumor. The result is that recurrences of such benign exostoses are by no means rare (5 per cent of this series), and when recurrence does not take place, the adjacent cortex often reforms in an irregular and troublesome manner (fig. 23).

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11. Geschickter, C. F., and Copeland, M. M., with foreword by Bloodgood, J. C.: Osteitis Fibrosa and Giant Cell Tumor, Arch. Surg. **19**:169 (Aug.) 1929.

While many exostoses do not require operation and cures are commonly effected in those with aggravated symptoms by simple surgical removal, there is a third group in which both the prognosis and the treatment are an entirely different problem. This is the group of benign osteochondromas which undergo secondary malignant change. In the present series of cases, malignancy arose in over 7 per cent of these benign exostoses or osteochondromas. This is a far higher percentage than is generally conceded, but the reason for this increase in the per-

Fig. 23 (P. N. 35720).—Roentgenogram taken ten months after complete excision of the exostosis shown in figure 4. Note the gradual reformation of bone escaping through the periosteal gap at the site of the former exostosis.

centage of malignancy in the present series is due to the method in which they were studied.

It is not sufficient to follow up the cases of benign exostoses and to find out in which of them the patients subsequently die of sarcoma developing in the original lesion. The usual benign exostosis which comes under the observation of the physician or surgeon is removed, and this removal usually eventuates in healing so that the possibility of malignancy is obviated. In patients discharged without treatment or

who have recurrence after removal there is, of course, the possibility of malignancy. But there is also a still larger group of cases that never come under the observation of any physician until malignant change has occurred. To determine this third group, it is necessary to examine carefully the roentgenograms and specimens in all cases in the osteogenic sarcoma group and to isolate those cases which show evidence of arising in a previous osteochondroma. It is this third group of cases (table 6) in which most of the osteochondromas terminating in sarcoma were found.

In view of this fairly large percentage of cases with malignant change, the question arises whether or not the removal of an exostosis is warranted as a preventive measure. Such a wholesale removal of these growths is not favored on the basis of the present study, but attention is called to the need of following cases in which operation has not been performed and of informing the patient to return at once if he observes any unusual increase in the growth or an aggravation of symptoms. In addition, tumors which are discovered in the roentgenogram in and about the pelvis or about the spine should be removed or followed by repeated roentgen examinations twice yearly because their location makes any increase in size dangerous to the patient.

While the age of the patient is a factor in the sarcomatous transformation of these neoplasms, it does not serve as a guide in the rendering of a prognosis. In persons between 15 and 20, the growth impetus following adolescence may stimulate these tumors directly, and in patients over 40 the loss of the proliferating powers in the periosteal regions of the exostosis makes stimulation by trauma or infection of the tumor more dangerous. This permits the malignant change to occur at almost any age.

MULTIPLE EXOSTOSES OR HEREDITARY DEFORMING CHONDRODYSPLASIA

In the foregoing discussion of osteochondromas or single exostoses, an analysis was made which emphasized not the cartilaginous or the osseous portions of these tumors, but instead, their derivation from a precartilaginous connective tissue concerned with periarticular functions. Although this precartilaginous connective tissue is visible only in remnants at the periphery of these tumors, it is nevertheless the mother substance of the cartilaginous mass that has received so much attention by other authors. This tendency to emphasize the chondral substance of these tumors instead of their connective tissue origin, particularly when they assume the form of the so-called multiple cartilaginous exostoses or hereditary deforming chondrodysplasia, has been the cause of much confusion in the attempts to interpret the nature of this multiple skeletal disease.

Hereditary deforming chondrodysplasia (a term given by Ehrenfried [3]) denotes a distinct clinical form of exostosis in which the multiple occurrence of such tumors in a single patient is accompanied by numerous other skeletal deformities, such as bending and shortening of the bones and widening and irregularity of their metaphyseal ends. This form of the disease known in the literature under many different terms is congenital, and is usually discovered in childhood. The hereditary factor is extremely prominent and has been traced through as many as four or five generations. The mode of transmission is direct but somewhat variable, and apparently both males and females may transmit the disease. The fundamental basis of the congenital disturbance is obscure, but deficiencies in the periosteum and a tendency for the perichondrium to persist and to function as such, together with precartilaginous connective tissue about the joints, seem to be responsible for most of the deformities.

CLINICAL FEATURES

Although the disease is active throughout the developmental period of skeletal growth, the actual age of observation varies according to the time when the physician is first consulted. Usually the patient comes under observation between the ages of 9 and 20, but the disease has been reported as early as the age of 4 years and as late as 80. The deformities affect primarily only the bones derived from cartilage and involve most markedly the bones of the forearm and foreleg, although the femur and humerus rarely escape. Most of the exostoses are found in the cortical region of the bone, resulting in a widening of the shaft at these points and giving rise at their base to areas of either increased or decreased density. In addition to the outward projections at these points, there may be an inward growth resulting in the formation of central chondromas. The last named have often been mistaken for cysts of the bone. Where two adjacent bones are affected, as the radius and ulna or the tibia and fibula, fusion may occur between the expanded and distorted areas of the cortex (fig. 24), the lesser bone (fibula or ulna) usually suffering arrested development.

In well developed cases, the outstanding symptomatology relates to the deformity or so-called "family mark," which consists in shortening of stature and crookedness of the arms or legs. As the disease progresses, one or more of the osteochondromas, because of continued growth, will impinge on important structures, causing pain and dysfunction. One of the common disturbances of such impingement is a resulting paraplegia or local paralysis. Exostoses about the spine may result in either a spastic or a flaccid paraplegia, while local growths in the region of the knee by pressure on the peroneal nerve may give rise to paralytic clubfoot. In rare instances, an aneurysm has developed as a result of a constant trauma to an adjacent vessel.

Variability characterizes the more marked symptoms of the disease. During the youth of the patient, painful growths may continue to arise, to decrease finally or nearly disappear after the patient reaches maturity. While the deformities tend to become stationary in adulthood, exacerbation of symptoms may be produced by local irritation to an under-

Fig. 24 (P. N. 28246).—Case of congenital multiple exostosis showing fusion between the lower end of the radius and the lower end of the ulna. Note the bending and distortion of the bones of the forearm and the undeveloped state of the distal end of the ulna.

lying growth. As pointed out for single exostoses, an increase in the severity of symptoms after the age of 30 in a previously dormant osteochondroma may be the first sign of a malignant change.

Unless neurologic manifestations are present, examination of the patient usually shows few systemic features of clinical interest other than those relating to the skeleton. Unlike chondrodystrophia fetalis, there is no alteration of the physiognomy and no deformity of the head, although congenital anomalies, such as a deficiency of the bladder sphincter, may be present. The bones of the trunk are usually not markedly involved by the disease, although exostoses affecting the spine and ribs are occasionally recorded. In the extremities there is a tendency for a fairly symmetrical bilateral involvement, although unequalness in the length of either arms or legs is not rare. Full extension is often limited, and there is bowing of the forearms and often of the forelegs. Deformities of the hands and feet, particularly in the phalanges, are common. Definite hard and knotty outgrowths attached to the bone may be palpated, usually near the ends of the bones but occasionally near the region of the midshaft. The quiescent growths are less than the size of a fist, but progressive osteochondromas in which malignancy may be suspected may exceed the size of a child's head.

ROENTGENOGRAPHIC FEATURES

In the x-ray films taken of this condition, numerous typical osteochondromas, involving the metaphyseal region of the long bones of the extremities, are found. These outgrowths may appear in clusters about a given region and beneath the point of these exostoses, the shaft of the bone is widened and the cortex frequently thinner than normal. The exostoses vary in configuration, some being of the pedicle type, others a cauliflower-like growth with a broad base, and still others rounded, elevated areas near the deformed end of the bone (fig. 25).

In the ulna or fibula, bending is usually marked, and there is an arrest of growth showing shortening and failure of the epiphyseal ends to develop properly (fig. 24). In the ulna, it is usually the lower end of the bone which is deficient, and it is in this region that fusion with the radius often takes place. In the fibula, the upper end is most frequently affected, and synostosis with the tibia may result. Although the entire end of a bone, such as the lower end of the ulna, may be distorted by these outgrowths and the thinning of the cortex, and the foamy area in the base of the exostosis may resemble a cyst, true cysts of the bone such as those seen in osteitis fibrosa have not been recorded in the present series, and to my knowledge there is no verified record in the literature of such a cyst despite several erroneous references recently published.

This is one of the easiest conditions in the entire bone tumor group to diagnose in the roentgenogram. The three salient features determining the diagnosis are: the formation of typical exostoses of the pedicle or broad base type, the widening of the metaphyseal ends of the long bones and the deformity with bending and fusion of the ulna or fibula.

in the forearm or foreleg. The appearance of the bones about the knee is typical (figure 25). The lower end of the femur is squared off, and the exostoses projecting therefrom are directed upward in the direction of the muscle pull. The upper end of the tibia is similarly distorted, the outgrowths in this instance pointing downward. The

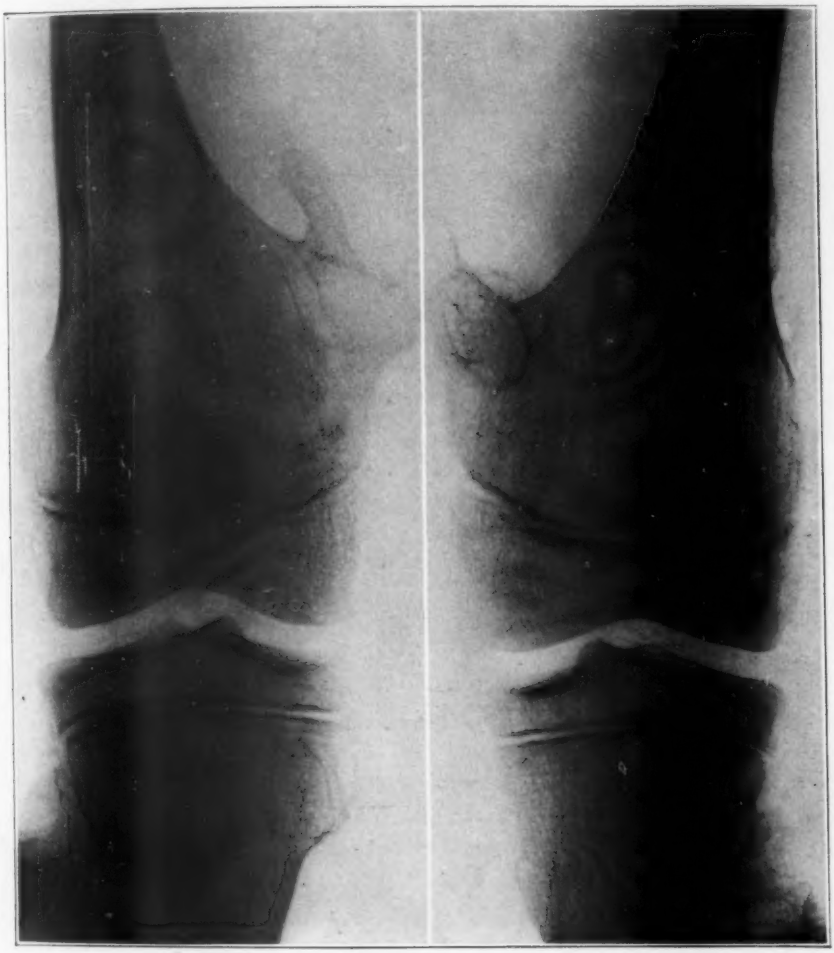

Fig. 25 (P. N. 28539).—The bones about the knee joint in a case of hereditary, deforming chondrodysplasia. In addition to the numerous exostoses, note the widening of the metaphyseal ends of the bone which gives to the lower end of the femur and upper end of the tibia a characteristic squared-off appearance.

upper end of the fibula is expanded and often fused with the end of the tibia.

The possibility of malignancy in these conditions is a much disputed point. If malignancy occurs, it is never generalized or multiple in

focus, but arises in a single osteochondroma, and for this reason differs in no way from the possible malignant change discussed under single exostoses.

Apart from the cases of typical hereditary deforming chondrodysplasia with its outspoken manifestations, there are occasional nonhereditary cases in which several cartilaginous tumors may affect a single bone or several widely separated bones. Rarely such instances are observed in which multiple chondromas of the hand are associated with exostoses in the arm or another long bone. More frequently, several exostoses in a single region of one bone have been observed. Associated with such a nest of lesions, there is the same metaphyseal widening seen, as in hereditary deforming chondrodysplasia, and there may also be bending and deformity of the bone. Such cases are best referred to as multiple exostosis or simple chondrodysplasia, and represent a transitional group of lesions midway between single osteochondromas on the one hand and multiple exostosis of the hereditary deforming chondrodysplasia type on the other.

PATHOLOGY

Adequate study of the gross pathology of these lesions is difficult owing to the scarcity of material. Since the disease is ordinarily not fatal and operation, when performed, is restricted to a single lesion, a detailed study of many bones has rarely been made. In general, the pathologic process of the local growths is the same as that described for the single osteochondroma. The important points of difference are the multiplicity of the tumors, the frequency with which cartilaginous masses are found embedded in the medullary and subcortical regions of the bone beneath the exostoses and the bending and distortion of the long bones, particularly the ulna and fibula (fig. 26).

The widening of the metaphyseal region and the distortion of the bone beneath the site of the exostoses are among the most interesting features of this condition of the skeleton. Many explanations have been advanced to account for these peculiarities, most of them relating the conditions either to a generalized disease, such as rickets, syphilis or tuberculosis, acting on the epiphyseal line or to a failure of the metaphysis to become modeled into a normal shaft because of some inherent and hereditary defect. The first group of explanations relating to the epiphyseal line and originating with Virchow have been gradually abandoned. The other group of explanations relating to the metaphysis are more current but are mostly theoretical without a true pathologic or embryologic basis.

Another of the more intriguing deformities is the stunting of the growth of those bones that do not bear direct strain or weight, such

as the ulna and fibula. The curious way in which these two bones are outstripped in size and growth by their neighbors, the radius and tibia, affords an important clue to the pathologic picture of the disease.

Microscopically, the duplication in the multiple exostoses of the histologic picture, described under single osteochondromas, indicates that the histogenic processes described in connection with those lesions also apply to the more diffuse form of this skeletal condition.

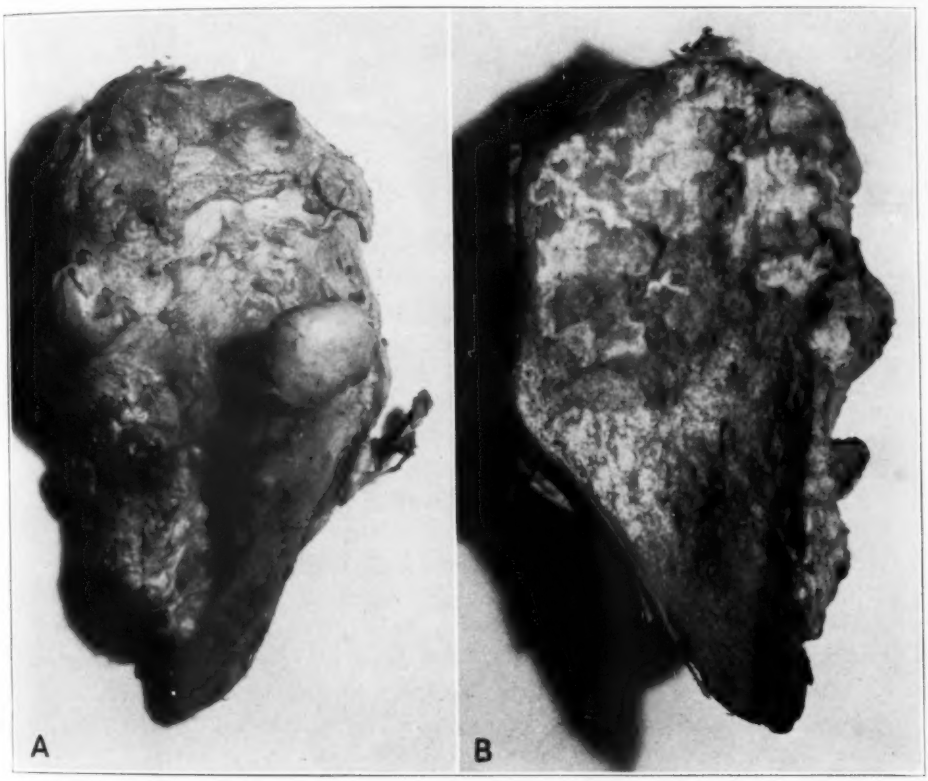

Fig. 26 (P. N. 19339).—Gross specimen from a case of hereditary, deforming chondrodysplasia after a resection of the upper end of the tibia and upper end of the fibula. The uncut surface (*A*) shows the numerous cartilaginous outgrowths and synostosis between the fibula and tibia. The cut surface (*B*) shows islands of chondromatous tissue extending into the epiphyseal and metaphyseal regions of the cancellous bone.

HISTOGENESIS

The formation of single exostoses as an exaggeration of a normal bony protuberance when maladjustment occurs between the periosteal cuff and the precartilaginous connective tissue embedded in the end

of the tendon suggests that in the condition of hereditary deforming chondrodysplasia, in which so many of these tumors are present, a similar disturbance affecting the periosteum and the precartilaginous connective tissue is present. In its earliest state, the bulk of the periosteum is in reality perichondrium, a tissue identical with the precartilaginous connective tissue which persists about the joints and in the ends of the tendons. It is clear, therefore, that if there is an arrest of development and a tendency for this precartilaginous tissue to persist not only in periarticular regions but also at points in the periosteum, the bones of cartilaginous origin will be affected throughout. This probably occurs in multiple exostoses. Not only do the periarticular points of primitive connective tissue act as sources for these cartilaginous growths, but, in addition, the periosteum at many points does not develop as such but is replaced by insufficient amounts of the more primitive perichondrium.

The failure of the periosteum to develop adequately, or rather its tendency to lag behind its normal rate of differentiation, has a multiplicity of effects on the bone beneath. Among other things, the cortex does not achieve its full thickness, owing to the absence of an adequate subperiosteal layer of osteogenic tissue provided with fully developed osteoblasts. In addition, the envelop formed by the periosteum is insufficient and incomplete, resulting in a failure of the periosteum to act as an efficient limiting membrane to growth of bone. Failure in this function as a limiting membrane leads to widening of the metaphysis and irregular protrusions through points of defect in the periosteum. The inadequacy of this line of limitation is most apparent in the fibula and ulna. In view of Wolff's [12] law, which states that the development of bone structure is in accordance with bone stress and strain, it is important to bear in mind that these accessory bones of the forearm and foreleg are not subjected to the direct stress received by the radius and tibia and therefore lack the corrective influence of their neighbors. As a result, the defects brought about by periosteal deficiency are accentuated.

The formation of exostoses akin to those found in cases of single osteochondroma are to be ascribed to the precartilaginous tissue in the tendon ends which does not form its destined junction with an outgrowing periosteal cuff. The irregular masses of cartilage found next to the cortex and growing inwardly are more likely due to persisting strands of primitive perichondrium. The entire process is extremely complicated, but it shows what a fine state of balance among various tissues of similar functions is necessary to produce the normal.

12. Wolff, J.: Ueber die inneren Architectur der Knochen und ihre Bedeutung für die Frage vom Knochen Wachstum, Arch. f. path. Anat. **1**:389, 1870.

PROGNOSIS AND TREATMENT

The prognosis for life in these cases is good, but there is no adequate form of treatment except operation for correction of deformities after the growth period has ceased. Most of the deformities, such as shortening of stature and unequal length of the bones of the extremities, usually give no indication for treatment, but exostoses causing neurologic manifestations, dysfunction in the use of limbs or injury to vessels should be promptly excised.

In two cases in this series secondary malignant change occurred in these cartilaginous growths resulting in death from chondromyxosarcomas. Other such cases with malignant change have been reported from time to time in the literature. The treatment of such sarcomatous growths is discussed in the chapter on secondary chondromyxosarcoma.

CHONDROMAS OR CHONDROMYXOMAS

A fairly common type of cartilaginous tumor, designated here as benign chondroma, resembles the exostoses histologically, but has not the same periosteal location or the same preponderantly osseous structure that is characteristic of the base or pedicle of the osteochondromas.

The typical chondroma is a benign lesion occurring in the small bones of the hands and feet or about the ribs and spine in patients between the ages of 20 and 30. In the phalanges of the hand where this tumor is most frequently located, the growth produces a central area of rarefaction in the affected bone which in the roentgenogram is visible as an expanded and cystic area within a shell of cortical bone. These chondromyxomas have been described as occurring commonly in the long pipe bones and about the pelvis in either a central or a periosteal location. However, in such locations these tumors are rarely of central origin, and of those of periosteal origin described as chondromas the majority are in reality osteochondromas with a large cartilaginous cap; they have been grouped under the exostoses in this paper (table 1). It is also essential to point out here that many of the chondromas growing to tremendous size, described as benign lesions in the literature, are essentially slowly growing chondromyxosarcomas arising secondarily in benign exostoses. This type of tumor is subsequently discussed in this paper under the heading of "secondary chondromyxosarcoma."

CLINICAL FEATURES

In the present series of seventy-one chondromyxomas (tables 2 and 3), males and females were about equally affected; the majority of the patients were white, and only two such lesions were recorded in Negroes. The curve of age distribution is shown in figure 27 and resembles the benign osteochondromas except that the peak of incidence is a decade later, between 20 and 30 instead of 10 and 20 years. The

predominant location, as shown in figure 28, is in the bones of the hands and feet, fifty of seventy-one lesions occurring in such localities. The ribs about the sternum in the region of the costochondral junction are next in order of frequency of involvement, and the region of the spine is also a common site.

The patient affected with a benign chondroma or chondromyxoma is most often an adult, who complains of recurrent soreness in a tumor of stationary or slowly increasing size located in one of the phalanges of the hand or foot. The symptoms are usually mild and protracted,

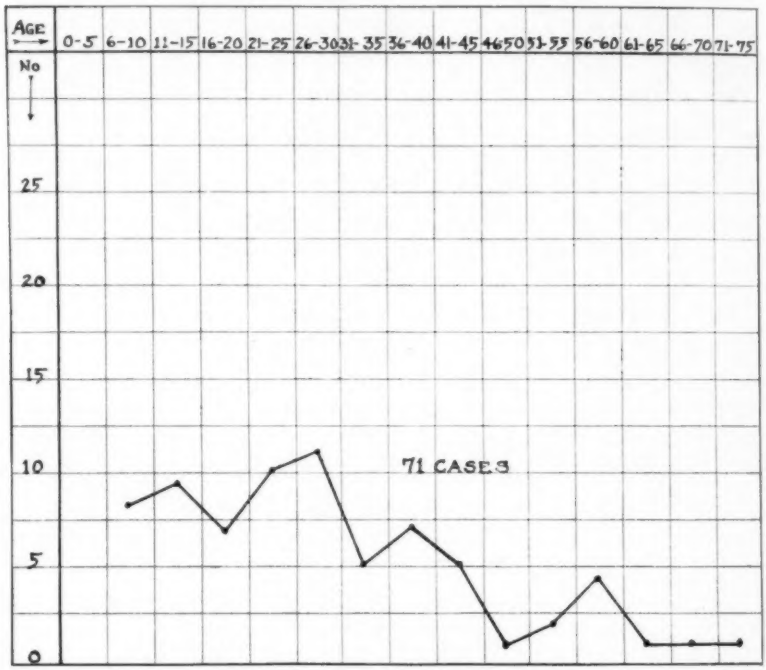

Fig. 27.—Chart showing age incidence of benign chondromas occurring in the small and large bones of the skeleton.

the clinical course extending on an average of over five years. Trauma is often recalled in connection with the initial appearance of the tumor and also again in connection with the exacerbation of the symptoms which brings the patient to the physician. Neither pain nor swelling is severe, the size of the tumor being in most instances less in diameter than a ten cent piece. Multiple involvement is not as frequent as one might infer from the literature. In the present series, only four cases of multiple chondromas are recorded, and in every one of these instances the diffuse involvement was in the hand or foot. However, in addition to the nodules, varying from three to ten in the small bones, there was in two of these cases an involvement of a long bone (femur or humerus).

The results of physical examination are usually negative, except for the local changes in the area of the tumor. Evidences of specific infections such as syphilis and tuberculosis have not been recorded, nor has bursitis been present in this series. The skin is usually unchanged, and the soft parts are freely movable over the tumor, which is firm to palpation, smooth or lobulated to the touch and securely attached to the adjoining bone. Pathologic fracture is present in 10 per cent of the lesions.

Fig. 28.—Incidence of chondromas according to skeletal location. The solid black areas indicate the most frequent sites; the dotted areas, the points occasionally involved.

About the ribs and sternum or when occurring centrally in the long bones, these growths may be of considerable dimensions and larger than an adult fist (fig. 29). In these larger growths a sudden increase in size or malignant change is far more frequent than in the small bones, and recurrence after a primary operation far more likely. Malignant change seems prone to occur in these larger tumors, particularly when they are associated with multiple chondromas in the small bones such as in the two cases just mentioned.

TABLE 2.—*Benign Chondromyxomas in Small Bones of the Hands and Feet*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment
45163	W	F	13	Multiple fingers and toes	Congenital	Tumor	Multiple rarefied areas	Excision, 1929	Myxoma; cartilage; bone	Discharged well
40424	W	F	30	Phalanx, ring finger	..	Tumor	.....	Curetted, 1929	.....	Discharged well
39758	W	F	10	Phalanx, right little toe	2	Tumor; pain	Central rarefied area	Curetted, 1927	New bone fetal cartilage	Discharged well
39538	W	F	39	Phalanx, right thumb	..	Pathologic fracture	Central expanded rarefied area	Curetted, 1927	.....	.....
38169	W	F	18	Phalanx, right little finger	72	Trauma; tumor	.....	Curetted, 1925	Cancellous bone; adult cartilage	Discharged well
37112	W	F	30	Metacarpal, right	48	Fracture; tumor	.....	Resection, 1925	Fetal cartilage; myxoma	Well 5 yr.
36660	W	F	32	Phalanx, middle finger	60	Trauma; tumor; pain	Central and cortical rarefied area	Curetted, 1925	Adult and calcifying cartilage	Well 4 yr.
36658	W	F	13	Phalanx, right forefinger	96	Trauma; tumor; pain	Central expanded rarefied area	Curetted, 1925	Cancellous bone; adult cartilage below myxoma	Well 4 yr.
36608	W	F	19	Phalanx, right finger	72	Trauma with repeated fracture	Rarefied area with fracture	Irradiated, 1924; operation	.....	Well 6 yr.
35942	W	M	46	Thumb, right	24	Trauma with dislocation	Ossified tumor in tendon	Excision, 1925	.....	Discharged well
35938	W	F	29	Middle phalanx, thumb	..	Pathologic fracture	Translucent area with ossification	Roentgen therapy, 1924	.....	Healing after 2 yr.
35504	W	M	9	Thumb and forefinger, left	36	Trauma	Multiple periosteal and central translucent tumors	.....	.....	Unchanged 6 yr. after
35308	W	M	19	Metacarpal, little finger	..	Tumor	Central rarefied area	Irradiation, 1924	.....	Some improvement 6 mo. later
35268	W	M	37	Phalanx, index finger	½	Trauma; pain	Central expanded rarefied area	Amputation, 1924	.....	Discharged well
34386	W	F	12	Phalanx, ring finger	24	Tumor	Central rarefied area	Observed, 1923; no operation	.....	Well 7 yr.
34058	W	F	40	Finger, left middle	..	Tumor	Central rarefied area	Excision, 1923	New bone; adult cartilage	Well 7 yr.
33152	W	F	12	Phalanx, ring finger	12	Tumor	Central and cortical rarefied area	Irradiation, 1922	.....	Unimproved; lost
33071	W	M	23	Phalanx, toe	¼	Trauma; tumor	Central expanded rarefied area	Amputation, 1923	Fetal cartilage; myxoma; new bone	Well 6 yr.
32848	..	..	..	Great toe	..	Tumor	Sesamoid bone	.....	.....	.....
32793	W	M	14	Phalanx, middle finger	24	Trauma; tumor; pain	Central expanded rarefied area	Curetted, 1923	.....	Well 6 yr.
30926	W	M	6	Phalanx, fourth finger, right	24	Tumor	Central and periosteal translucent area	Excision, 1922	Dense myxoma; fetal cartilage	Discharged well

30872	W	F	..	Phalanx, index finger	18	Tumor; pain	Sesamoid bone (?)	No operation; observed, 1922	.....	Well 8 yr.
29647	W	M	30	Phalanx, thumb	24	Trauma; tumor	Central rarefied area	No operation; observed, 1922	.....	Unchanged
29604	W	F	35	Phalanx, ring finger	168	Trauma; pain	Central rarefied area	No operation; observed, 1922	.....	Well 6 mo.; lost
29326	W	F	31	Phalanx, fore-finger	96	Trauma; tumor; pain	Central rarefied area	No operation	.....	Unchanged
29245	W	F	10	Fifth, metacarpal	36	Trauma; tumor; pain	Central rarefied area	Curetted, 1921	.....	Well 6 yr.
29239	W	F	30	Phalanx, thumb	..	Tumor	Central rarefied area, cortex roughened	Amputation, 1921	Fetal cartilage; myxoma	Well 8 yr.
29010	C	M	10	Phalanx, big toe	3	Tumor	Central expanded rarefied area	Amputation, 1921	Hyalinized cartilage	Well 7 yr.
28464	W	M	23	Phalanx, index finger	60	Tumor	Central rarefied area	Curetted, 1921	New bone; fetal cartilage; myxoma	Well 9 yr.
28365	W	M	27	Third, metacarpal	84	Heel fracture	Central expanded rarefied area	Curetted, 1921	New bone; fetal cartilage; myxoma	Well 9 yr.
27696	W	F	42	Phalanx, ring finger	24	Pain; tumor	Periosteal translucent area	Excision, 1921	New bone; fibrous tissue	Discharged well
26622	W	M	39	Phalanx	48	Trauma; tumor; pain	Periosteal translucent area	Excision, 1920	New bone; calcified and fetal cartilage	Well 9 yr.
26259	W	F	75	Phalanx, little finger	48	Tumor	Central expanded rarefied area	Amputation, 1920	New bone; fetal cartilage; myxoma	Well 8 yr.; dead 1928, heart disease
25646½	W	M	70	Third metacarpal	..	Limitation of motion	Multiple rarefied areas	Amputation	Adult and calcifying cartilage	Discharged well
25254	W	M	22	Phalanx, third toe, left	½	Trauma with pathologic fracture	Central expanded rarefied area	Amputation, 1918	.....	Well 1 yr.; lost
23886	W	M	35	Phalanx, little finger	48	Trauma; tumor; pain	Periosteal translucent area	Excision, 1918	New bone; calcified and fetal cartilage; myxoma	Discharged well
20944	W	F	25	Phalanx, ring finger	12	Tumor	Central expanded rarefied area	Curetted, 1919	Adult and calcified cartilage	Discharged well
16554	W	M	32	Metacarpal, middle finger	168	Trauma; tumor	Periosteal translucent area; new bone	Excision, 1924	Cancellous bone; adult cartilage	Well 10 yr.
15597	W	M	62	Phalanx, ring finger	240	Trauma; tumor	.....	Amputation, 1914	.....	Well 14 yr.
14552	W	F	15	Third metacarpal	12	Trauma; tumor	Central rarefied area	Resection, 1912; excision, 1913	Fetal cartilage; myxoma	Well 5 yr. after recurrence
12206	W	F	30	Phalanx, index finger	336	Trauma; tumor	.....	Curetted, 1911	.....	Discharged well
8630	W	F	22	Phalanx, little finger	60	Tumor	.....	Excision, 1907	Fetal cartilage; myxoma	Well 13 yr.
6892	W	F	40	Phalanx, middle finger	12	Tumor	.....	Amputation, 1901	Fetal cartilage; myxoma	Well 3 yr.; lost, 1930
6530½	W	F	24	Phalanx, ring finger	..	Tumor	.....	Excision	.....	Discharged well
730	W	M	58	Phalanx, toe	324	Trauma; tumor	....	Amputation, 1890	.....	Discharged well

TABLE 3.—*Benign Chondromas in Large Bones*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment
38196	W	M	19	Os calci	60	Pain; tumor	Small rarefied areas	Curetted, 1926	.....	Well 4 yr.
42985	C	F	8	Radius, styloid	..	Tumor	.....	Excision, 1928	Cartilage in tendon	Discharged well
41435	W	M	24	Rib	..	Tumor	.....	Excision, 1927	Adult cartilage	Discharged well
37746	W	M	25	Os calcis	½	Trauma; tumor; discharging sinus	.....	Drained, 1926; amputation advised	.....	Unimproved
40657	W	M	14	Vertebra	..	Tumor	.....	Excision, 1927	Cartilage	Discharged well
38968	W	F	19	Symphysis pubis	108	Trauma; tumor	Central destruction of bone	Irradiation, 1927	.....	Lost
38931	W	F	26	Sternoclavicular joint	150	Tumor; pain	.....	Excision, 1926	Hypertrophied joint cartilage	Discharged well
38002	W	M	10	Rib, second, left	120	Trauma; tumor	Cystic periosteal shadow	Irradiation, 1926	.....	Well 4 yr., 1930
36808	W	M	7	Femur, left, lower	12	Pathologic fracture, twice	Subcortical rarefied area with fracture	Osteotomy; amputation, 1925	Joint cartilage; bone	Lost, 1925
34502	W	M	55	Sacrum and lumbar vertebra	180	Trauma; pain; tumor	Lobulated mass	Coccyx resected	Myxoma; cartilage	.....
32482	W	M	43	Sternum	132	Trauma; tumor	Central expanded rarefied area	Observed, 1915; roentgen therapy prescribed	.....	Signs of malignant change, 1930
32415	W	M	22	Humerus, shaft, left, pathologic	48	Pain; tumor	Central expanded rarefied area, roughened	Amputation, 1923	Cancellous bone; fetal cartilage	Discharged well
30173	W	M	15	First lumbar vertebra	24	Pain	Periosteal translucent area	Excision, 1915	Cancellous bone; adult cartilage	Well 7 yr.
29814	W	F	16	Ribs, third and fourth	30	Tumor	Rarefied area	Observed, 1922; no operation	.....	Well 8 yr.
26287	W	F	40	Humerus, upper, left	12	Tumor	.....	Excision, 6 times, 1915 to 1919; amputation, 1920	Chondroma; adult cartilage	Recurred, well 10 yr. after
23047	W	F	30	Rib, third, sternal end	..	Tumor	.....	Excision, 1918	Adult cartilage	Discharged well
22016	W	F	51	Femur, lower	84	Tumor; pain	Subcortical expanded rarefied area	Excision, 1917	Adult cartilage; hyalinized fibrous tissue	Well 6 yr., lost, 1930
19545	W	M	43	Os calcis	12	Pain; tumor	Central rarefied area	Curetting, 1916: amputation, 1919	.....	Recurred, well 6 yr. after
18751	W	M	51	Ninth dorsal vertebra	12	Pain	.....	Excision, 1915 and 1916	Cancellous bone; adult cartilage	Dead; second operation
17112	W	F	44	Rib	..	Tumor	.....	Excision, 1913, twice; excision, 1914; treated by radium	Adult cartilage; new bone	Well 8 yr.; dead of tuberculosis
15395	W	M	49	Sternum, upper	36	Tumor	.....	Partial excision, 1914	.....	Well, 1923
13790	W	M	14	Ulna, head	4	Tumor; pain; stiffness	Translucent periosteal mass	Excision, 1913	Adult and calcified cartilage; myxoma	Well 9 yr.
11342	W	M	20	Thigh	48	Tumor; pain	Translucent soft part; shadow	Excision, 1911	Adult cartilage; laminated bone	Well 11 yr.
10407	W	F	24	Ribs, third, right	12	Tumor; pain	Translucent expanded area	No operation	.....	.....
8192	W	M	35	Fifth rib	..	Tumor	.....	Excision, 1908	.....	Recurred
8111	W	M	56	Os calcis, right	36	Tumor	.....	Excision, 1907	Adult cartilage; myxoma	Recurred in 1 yr.
908	W	M	70	Humerus, upper	13	Trauma; tumor; fracture	.....	Amputation, 1895	Adult; fetal cartilage; myxoma	Dead, other causes 13 yr. later

ROENTGENOLOGIC FEATURES

In the roentgenogram a typical chondroma is a small, translucent and rarefied area occurring centrally in the shaft of a small bone. The cortex about the lesion is thinned and expanded, inviting pathologic fracture. Unlike the osteochondromas, neither new bone formation nor calcification is marked in these small lesions, although trabeculae traversing the tumor (composed of hyalinized fibrous tissue) may be

Fig. 29 (P. N. 32482).—A large chondroma of the sternum present for over fifteen years in a white man, aged 43. This tumor was first observed in 1915, and roentgen therapy was prescribed. Roentgenograms of this lesion are shown in figure 32. Despite repeated irradiations, the most recent x-ray films depict a change suggestive of malignancy.

visible in the x-ray film. Perforation of the bone shell with extension of a translucent shadow into the soft parts is not rare (fig. 30).

The benign chondroma is the most frequent lesion producing a central area of bone destruction in a phalanx. Bone cysts and giant cell tumors, which may occur in the small bones of the hands and feet and produce a similar picture in the roentgenogram, are more common in the metacarpal and metatarsal bones and are rarer in the phalanges.) It is also helpful to bear in mind that multiple giant cell tumors or bone

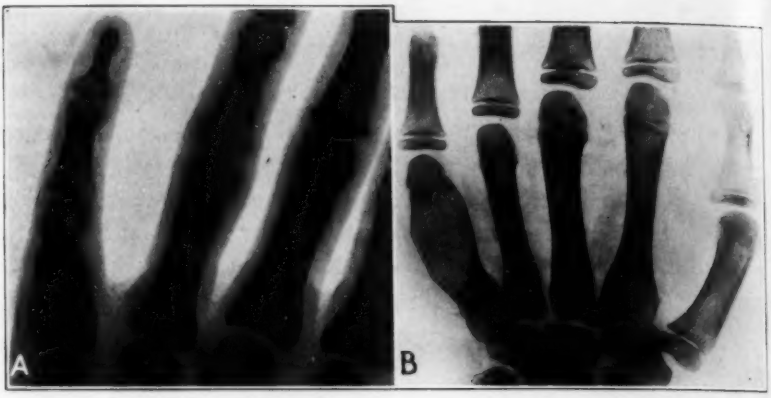

Fig. 30.—*A* (P. N. 29326) shows a central chondroma in the phalanx of the forefinger in a woman 31 years old. The appearance of this tumor followed trauma eight years previously. The cortical bone is intact, and the periosteal zones are not involved. *B* (P. N. 29245) shows a central chondroma occurring in a metacarpal bone in a girl, aged 10. This lesion also followed trauma three years previously, but was effectively treated with curetting and has remained well over six years.

Fig. 31 (P. N. 35336).—A roentgenogram showing the multiple punched-out areas due to gout occurring in the hand of a white man over 50 years of age. Other joints in the body were affected, and recurrent attacks of acute arthritis were present.

cysts are practically unknown in the small bones of the extremities. However, multiple punched-out areas of bone destruction which are not encapsulated by a shell of cortical bone in these localities may be produced by gout (fig. 31). Metastatic carcinoma and multiple myeloma practically never affect these small bones, unless the rest of the entire skeleton is riddled with the disease.

The majority of the larger tumors of the chondroma class are situated about the sternum at the costal chondral junctions or within the body of this bone. In this location they produce a gnarled mass of rubbery consistency which is difficult, because of its location, to visualize

Fig. 32 (P. N. 32482).—*A* shows the central chondroma of the sternum shown in figure 26. The roentgenogram was made eight years after the first observation, and although the lesion has grown the bone shell is still intact and the tumor is outlined by a definite calcified margin. *B* shows the same lesion five years later. Note the spotting and beginning granular appearance of the lesion and the extension beyond the bone shell. Because of the spotting and the hazy margins of the growth, this picture is suggestive of an early malignant change. Such a malignant change is very common in chondromas of the large bones after they have persisted for many years in a benign state.

clearly in the roentgenogram. The diagnosis, however, can usually be made from the location of the lesion and by the expansion of the bone which occasions no great amount of destruction or erosion. The absence of an infiltrating shadow in the periosteal zones is against the presence of malignancy in these cases (fig. 32).

True central chondromas of the long bones are extremely rare, and it is doubtful whether such a diagnosis is justified on the basis of the roentgenogram alone. In nearly 2,000 tumors of the bone there are but 5 well established cases, and in these, the resemblance is so close to malignancy in the x-ray film, and the tendency for the lesion to recur and to be cured only by radical operation is so great that there is little practical harm in classing these tumors as forms of chondrosarcoma,

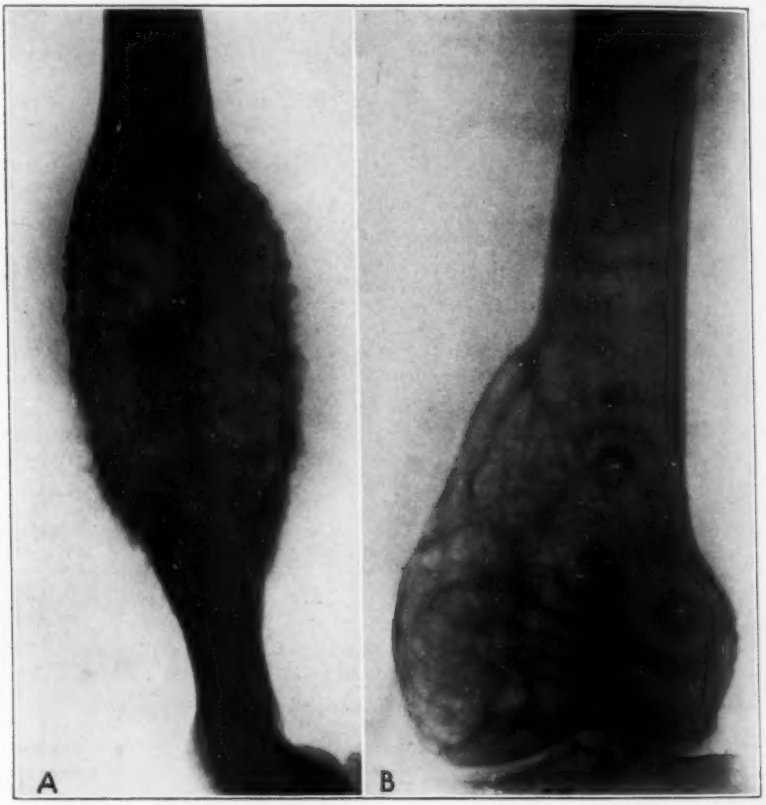

Fig. 33.—*A* (P. N. 32415) shows a large central chondroma in the shaft of the humerus. The symmetrical nature of the expansion resembles a benign bone cyst, but the multilocular markings of the cavity and the peculiar roughness extending beyond the shell of cortical bone suggest a central chondroma which is extremely rare in the long bones. *B* (P. N. 22016) shows a rare central chondroma occurring in the epiphysis of the lower end of the femur. This resembles somewhat in appearance a benign giant cell tumor, but it has again the characteristic multilocular appearance of a chondroma. This is also a rare type of lesion in this location.

although those not experienced may be misled into an erroneous diagnosis of cyst of the bone. Nevertheless, from a scientific standpoint, the possibility of the occurrence of a true central chondroma in the long

bones must be conceded, and I have reproduced the illustrations of the roentgenograms of several of these cases as more or less of a curiosity. The only distinctive roentgen features are the tendency to expand the bone, the marking of the translucent areas by lines and particles of calcification which produce a distinctly multiloculated effect and the involvement of the periosteal region by peculiar roughened areas escaping beyond the cortex (fig. 33).

GROSS PATHOLOGY

The outstanding characteristics in the gross specimens of neoplasms composed primarily of cartilage are the lobulated and gelatinous character of the growth. The tumor is always composed of numerous pockets, marked off by visible fibrous trabeculae, and within these pockets there is a typical translucent and congealed substance of more or less rubbery consistency, which under the microscope can be identified as cartilage. Variation in this lobulated and gelatinous appearance depends on the size of the tumor. In the small bones, the capsule containing osseous material lends a firmness to the tumor, and in addition, calcification may aid in solidifying the mass. Elsewhere in the large bones where the tumor attains a greater size, there is a tendency to cystic change in the pockets of the lobules, and these cysts may contain a syrupy fluid which pours from the tumor when it is sectioned (fig. 34).

The color of the tumor varies from a pearly gray to light yellow. Occasionally small foci of hemorrhage may discolor the tumor with deep red or black. However, these growths are not vascular, and the vessels described in the literature, particularly under the old terminology of angiochondroma, are to be found in the adjacent soft parts and not in the tumor proper.

In the small bones the structure of the chondroma is fairly characteristic. In most instances the bone is intact (fig. 35), and portions of the cancellous bone usually remain in one or more areas, either forming the boundary of the tumor at one end or projecting into the tumor at one or more points as the remains of the original medullary structure. Within such bony confines the gelatinous mass infiltrates everywhere as if it had been poured into a mold and left there to congeal and harden. Within the congealed substance, a few gritty areas of calcification may be felt.

About the ribs or spine these growths are firm, nodular masses which become cystic when attaining to large size. In the rare instances in which these tumors involve a long bone, they show greater proliferative powers, and the original mass is reduplicated by similar clusters of lobules. Some of these reduplicated masses may be uniformly gelatinous, others are cystic and exude fluid from their smaller pockets. These

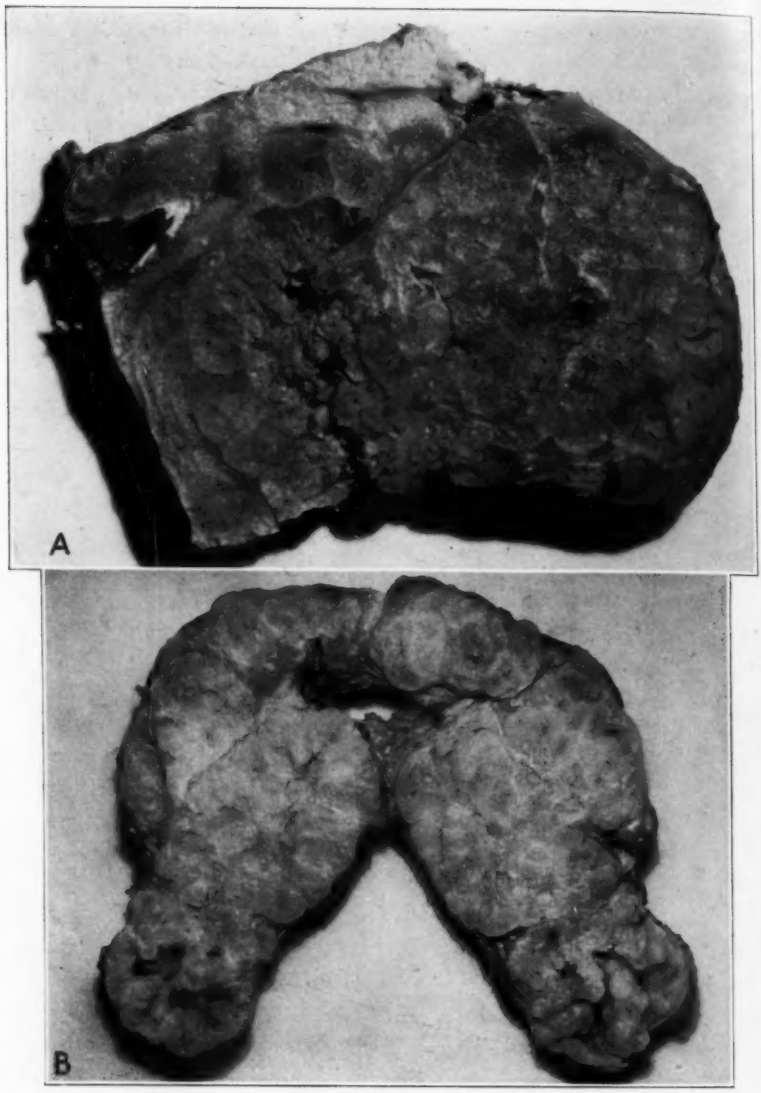

Fig. 34.—Gross specimens of two recurrent chondromatous lesions of the large bones in patients who have remained well for over five years. *A* (P. N. 26287) shows a lobulated tumor mass from a central chondroma of the upper end of the humerus, and *B* (P. N. 25766) a similar tumor mass with cystic changes associated with an exostosis in the lower end of the femur. These lesions illustrate the prognostic paradox in benign chondromas. The chondromas in the large bones, although typically benign under the microscope, have a decided tendency to recur and undergo malignant change, whereas chondromyxomas of the small bones, although resembling a malignant condition under the microscope, are clinically benign.

larger tumors of the benign chondroma class are difficult to distinguish in the gross (or even under the microscope) from chondromyxosarcomas, and because of their clinical behavior must be looked on as potentially malignant.

Fig. 35 (P. N. 33071).—Low magnification of a central chondroma occurring in the terminal phalanx of a toe. The lobulated tumor mass is encapsulated by a thin shell of bone.

MICROSCOPIC FEATURES

The bulk of the benign chondroma is composed of fairly normal adult cartilage. Under the microscope, this chondral substance shows a matrix of hyaline material divided into lobules by acellular strands of

eosin-staining connective tissue. The cartilage cells lie in pairs or tetrads, in small lacunae, and the nuclei, which readily undergo pyknosis, are surrounded by a generous amount of eosin-staining cytoplasm.

Variations of this typical structure depend on the location of the tumor. About the ribs and spine, the hyaline substance is much increased, the lobules are larger with fewer strands of connective tissue and the cartilage cells are sparse. This type of chondroma resembles

Fig. 36 (P. N. 22016).—Photomicrograph of a chondroma in a large bone The cellular connective tissue from which the chondroma is derived is shown at the margin overlying the tumor proper. The lobulated areas of adult cartilage are shown below. Note the sparsity of cellular material and the large amount of hyaline substance.

in its structure normal joint cartilage, and in all probability some of these tumors are hypertrophied and distorted masses from the costochondral junction (fig. 36) or vertebral disks.

In the rare instances of large chondromas in the long bones, necrosis and spotty calcification in the cartilage may be found. Connective tissue

cells are more frequent in the strands which mark off the lobules, and occasional islands of hyaline material in which fetal instead of adult cartilage cells are found are more likely to be seen (fig. 37).

In the small bones, the microscopic picture is changed by the manner in which the capsule infiltrates from the margin. Here there is much cellular connective tissue and fetal cartilage intermingled to form typical myxoma. In addition, the connective tissue at the margin of these

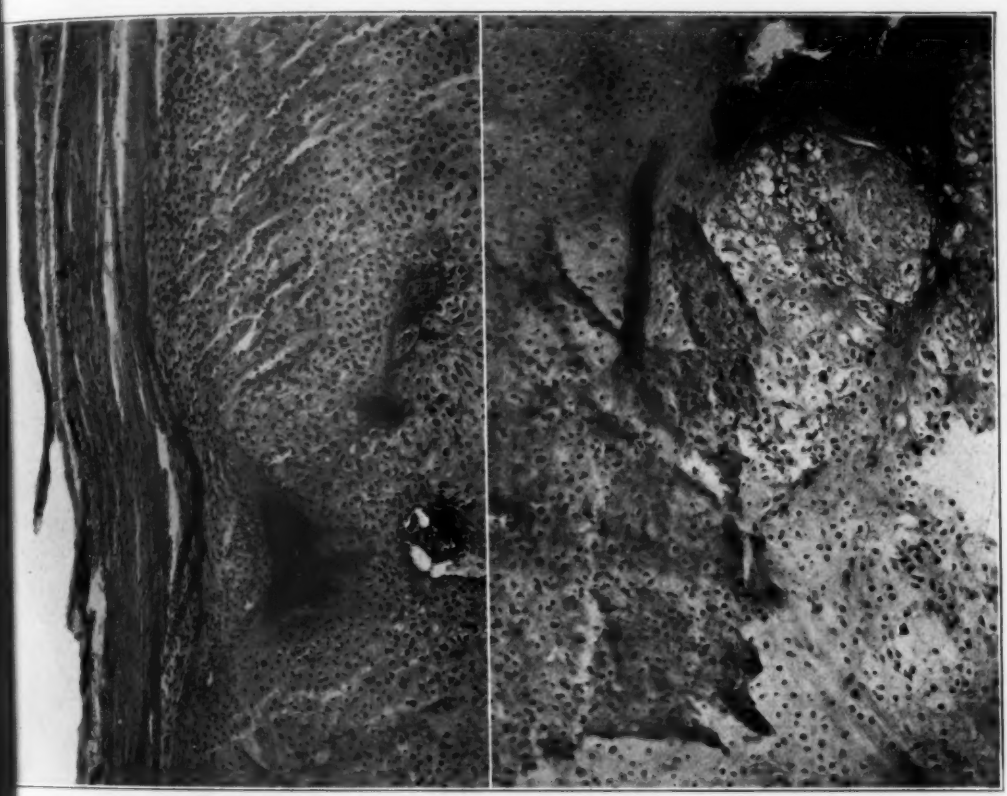

Fig. 37 (P. N. 38666).—Photomicrograph of a cellular area at the margin of a chondroma of a large bone. Numerous spindle cells are present in the connective tissue, and many of the cartilage cells are of the fetal type. An area of spotty calcification is seen. This lesion was in a white woman, aged 37, who had two unsuccessful curettings followed by amputation. The patient is living four years after the first operation. This picture demonstrates the borderline type of chondroma in which the exact onset or presence of malignant transformation cannot be determined. Clinically, the lesion has been tabulated with chondromyxosarcoma arising secondarily in a benign chondroma.

tumors, which gives rise to such myxoma, shows definite ossification with the formation of islands of new bone. This transition from cellular connective tissue to myxoma to cartilage with a parallel production of

new bone is more typical of chondromyxosarcoma. In fact, if it were not for the location of these tumors in the small bones and their encapsulation, the diagnosis of benign chondroma or benign chondro-

Fig. 38 (P. N. 23886).—Photomicrograph of a central chondromyxoma of the small bones showing the more cellular areas which are responsible for the origin of the tumor. Dense strands of connective tissue can be seen giving rise to fetal and adult cartilage cells. Cartilage is undergoing calcification at one point.

myxoma from a microscopic standpoint would have to be changed to that of sarcoma (fig. 38). But in this respect the microscopic picture in these cartilaginous growths is misleading, since the tumors of this

type in the small bones of the hands and feet are, on the basis of clinical evidence, uniformly benign, while the chondromas in the larger bones (sternum, ribs, long bones, etc.) are potentially malignant despite a more benign histologic appearance.

When a large group of tumors of the benign chondroma class is reviewed microscopically in connection with the sections of many cases of exostosis and also many cases of chondromyxosarcoma, it can be seen that these tumors as a group represent a borderline or transition between the osteochondromas, on the one hand, and the chondromyxosarcomas, on the other.

All of these tumors show the same transition from cellular connective tissue to myxoma with fetal cartilage to adult cartilage with a parallel formation of new bone from connective tissue. In benign osteochondromas, the bone formation predominates, the cartilage is adult cartilage, and strands of active connective tissue and myxoma can be located only as insignificant remnants in the capsule of the tumor by the use of the high power of the microscope. In the benign chondromas, adult cartilage and not bone predominates. In the strands of connective tissue which divide the chondroma into lobules, myxoma and fetal cartilage is nearly always absent, but in the strands of connective tissue which form the capsule, this tissue is easily found. Particularly in the small bones is fetal cartilage a common occurrence, and myxomatous areas along with new bone formation are the rule in the margin of these small growths. In chondromyxosarcoma, the cellular strands of connective tissue giving rise to myxoma with fetal cartilage infiltrate everywhere, and islands of abortive cartilage with malignant nuclei of the vesicular type are replaced at intervals by areas of new bone formation.

A graded series of histogenic changes in these tumors can thus be traced, the amount and degree of cellular activity in the primitive connective tissue, which is the mother substance of these growths, indicating in a general way the degree of the malignancy.

HISTOGENESIS

Most of the chondromas and chondromyxomas represent histogenetically supernumerary joint cartilages. In the regions in which they predominate—the hands and feet, the spine, ribs and sternum—there are far more joints and articular surfaces than elsewhere in the body. Embryologically, these joints are laid down by strands of primitive precartilaginous connective tissue which cut across the axis of the future bones at right angles (fig. 39). These precartilaginous strands are the same type of primitive connective tissue that forms the osseous ends of tendons and gives rise to the abnormalities of exostoses and osteochondromas. This accounts for the similarity histologically between the chondromas and the exostoses. In forming the joints, this pre-

cartilaginous tissue normally undergoes mucoid regressive changes to form the synovial lined joint cavities. However, aberrant persisting strands which do not thus regress are responsible at a later date for the origin of cartilaginous islands in the bone which form the chondromas and chondromyxomas. It is for this reason that the chondromas are found most frequently in a central location in bones in the regions of the body where there are the greatest number of joints.

The persistence of such precartilaginous tissue about the joints, particularly at the point of reflexion of the joint capsule may be demonstrated in normal adults (figs. 13 and 14). Neoplastic tendencies in

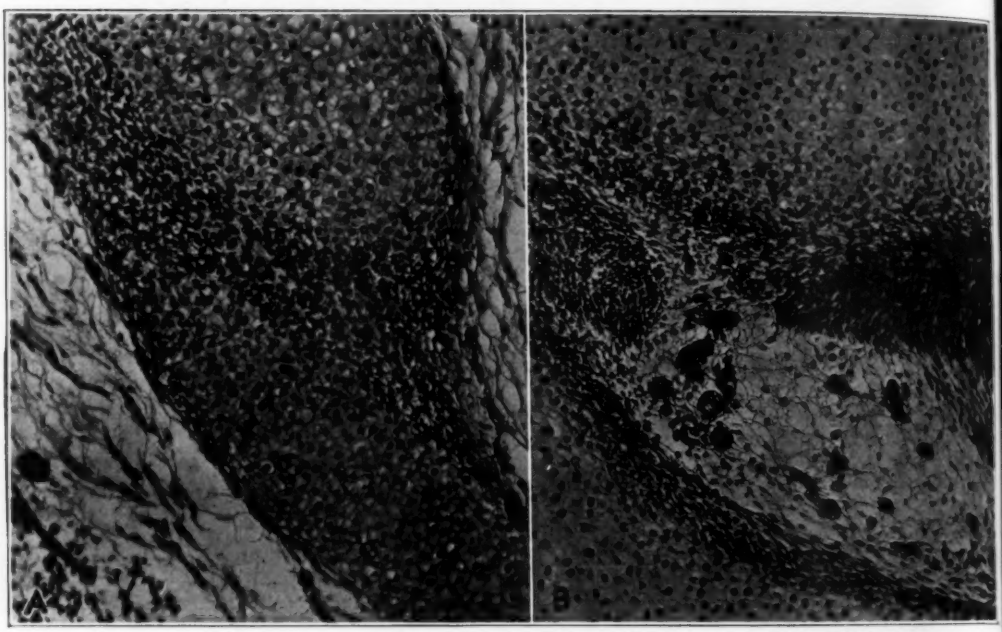

Fig. 39.—Photomicrographs showing the development of joint cavities in a human embryo 14 cm. in length. At *A*, the dense strands of embryonic connective tissue are cutting across the axis of the bone which is preformed in cartilage at the site of the future joint cavity. At *B*, this dense connective tissue is undergoing mucoid regression to form the joint cavity, and the capillaries of the future synovia are forming.

such tissue are shown in cases of osteochondromatosis of the knee joint (fig. 19), and the potentialities for continued growth are indicated in the chondro-osseous nodules formed in these regions in chronic infectious arthritis. The most conclusive evidence, however, is the appearance in these chondromatous tumors of so-called pure myxoma tissue, which is a histologic duplication of the regressive mucoid changes observed in the embryo during the formation of the joint cavities. This

myxomatous character is particularly prominent in the chondromas of the small bones and in those chondromatous lesions of the large bones undergoing secondary malignant change (fig. 66).

From a practical point of view, it is of importance to understand, if possible, why the chondromas should present a more cellular and myxomatous appearance when they occur in the small bones and yet remain in this location so uniformly benign; and why, on the other hand they should be more predominantly cartilaginous when occurring in the long bones and yet more prone to malignant change. The explanation is to be found in the capsular changes. In the small bones, the cartilaginous center of the tumor never extends far from the influence of the cortical and periosteal margin of the growth, owing to the limitations of space. Thus the myxomatous strands characteristic of the margin of the chondromas are always readily visible among the cartilaginous areas. At the same time, normal periosteum with its subperiosteal osteogenic layers is capable of reacting to the tumor and laying down a protective shell of new bone (fig. 35), favoring a benign course in these smaller growths.

In the large bones, the conditions are reversed. The more central lobules of cartilage grow and reduplicate at some distance from the periosteal and capsular margin of the tumor. Cellular connective tissue strands and reactive new bone are therefore less likely to find their way into the chondral substance of the tumor. Therefore, within the chondroma, daughter lobules arise which are remote from the sphere of influence of cortical bone, and hence are more prone to sarcomatous change. For, from a study of various types of tumors of the bone (Geschickter and Copeland [13]), there is reason to believe that the potentialities for malignancy increase as the power of reaction in normal cortical bone decreases and its sphere of influence becomes remote.

PROGNOSIS AND TREATMENT

When these benign cartilaginous tumors are quiescent and give mild or no symptoms, they are best let alone and kept under observation by repeated roentgen examination. If because of their position they are frequently subjected to trauma, resulting in soreness and discomfort to the patient, their complete surgical removal should be undertaken, if this is feasible and the tumor is not too large. In the phalanges the lesion is usually small enough to permit preservation of the continuity of the bone after thorough curetting followed by cauterization. The ease with which this tumor tissue is transplanted in the wound with resulting recurrence, however, should constantly be kept in mind.

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13. Geschickter, C. F., and Copeland, M. M.: Tumors of the Bone, Internat. S. Digest **10**:323 (Dec.) 1930.

Recurrence is not frequent following operation on chondromas in the small bones. Approximately one third of the cases in this series were treated by primary amputation or radical resection, and in all such cases a permanent cure was affected. When curettement is followed by adequate cauterization, either thermally or chemically with 50 per cent zinc chloride, permanent cures have been established in such lesions occurring in the bones of the hand or foot.

In the chondromas occurring in the large bones, recurrences have followed operation in approximately 25 per cent of the cases. In some of these instances the growth returned after repeated partial excisions when the neoplasms, because of location, could not be completely removed. It is important to record here that patients followed from five to ten years after the first observation have remained well without treatment, although in some instances, such as the case shown in figure 32, there has been a gradual increase in the size of the tumor and recent evidence of malignant change.

When a previously quiescent tumor shows sudden signs of increased growth, with an exacerbation of symptoms, immediate and complete removal is indicated, as secondary malignant change is to be expected. In the instances in which the patient has been so unfortunate as to neglect the growth and allow the tumor to become of unusual size, or in which the location about the sternum or spine makes complete removal difficult or dangerous, partial excision followed by radium therapy should be attempted. The clinical follow-ups on the malignant cases arising from previous benign tumors of this group warrant a trial of thorough irradiation by means of radium. A favorable prognosis can usually be given unless the tumor is of the type just discussed and is too large or in too vital a location to permit complete removal.

In deciding whether a particular lesion in this group is to be treated from the benign or malignant standpoint, the location and not the pathologic changes must be given primary consideration. Chondromas occurring in the small bones of the hand or foot (the os calcis excepted), regardless of their pathologic appearance, may be looked on as benign lesions, curable by thorough extirpation (curetting and cauterization). True chondromas of large size occurring about the sternum and spine or in the long bones, regardless of their microscopic appearance, must be looked on as potentially malignant, and their surgical removal, if indicated, should be followed by radium therapy.

PRIMARY CHONDROMYXOSARCOMA

There is a divergence of opinion in the literature concerning the relationship of simple exostoses and benign chondromas to sarcoma. Cases of so-called malignant degeneration in chondromatous tumors have been cited from time to time in the older literature and have been estimated as occurring in about 5 per cent of congenital exostoses.

More recently, Hyndman [14] questioned such a conclusion and has stated that there "seems to be no evidence except possibly in a single instance, that any of the malignant changes (in the literature) are other than chondromatous or osteochondromatous." Bloodgood has been quoted in support of this statement.

There is possibly some room for doubt if attention is focused on the benign exostoses or chondromas and a search made among these lesions for instances in which secondary malignant change has resulted in metastases and death. Even from such a point of view there are undoubtedly cases in which death accompanied by generalized metastases has occurred, as will be demonstrated in the subsequent discussion of secondary chondromyxosarcoma. However, if one assumes an entirely different method of approach, beginning with an analysis of the various forms of osteogenic sarcoma, and seeks to determine on a histogenic basis whether or not sarcoma of such types is possible in the kind of neoplastic tissue responsible for exostoses and chondroma, the entire matter can be settled with little room for speculation or question.

The greatest number of tumors in the group of osteogenic sarcomas contain cartilage in association with a type of myxomatous connective tissue, indicative of a mode of origin analogous to the benign exostoses and chondromas (Geschickter [15]). As in the foregoing analysis of the benign lesions, this form of connective tissue can be traced to a survival at points in the skeleton of primitive perichondrium and periarticular strands of a similar precartilaginous tissue.

The relationship of these chondral forms of osteogenic sarcoma to the benign tumors of the fibrocartilaginous group is, therefore, an intimate one, and the true basis of origin among these various neoplasms is so nearly identical that it is often impossible, even with all the data at hand, to predict whether the outcome of the growth will be benign or malignant.

However, among these lesions there is a primary form of chondromyxosarcoma which shows from the start its sarcomatous bent. It is a very malignant tumor arising periosteally, which does not at the onset involve either the cortex or the medullary cavity of the bone (fig. 40), and which in the roentgenogram is characterized by its translucent and nearly invisible periosteal shadow. The distinguishing microscopic composition of loose myxomatous connective tissue merging into zones of fetal cartilage and chondral areas with an abundant hyaline matrix fringed by osseous tissue indicates its proliferative powers, yet identifies this sarcoma with the more benign tumors of the fibrocartilaginous group.

14. Hyndman, O. R.: Hereditary Deforming Chondrodysplasia: Report of a Case, Arch. Surg. **21**:12 (July) 1930.

15. Geschickter, C. F.: Osteogenic Sarcoma, Arch. Surg., to be published.

CLINICAL FEATURES

The clinical features of primary chondrosarcoma reflect in part the primitive histogenesis of this neoplasm. The frequency with which Negroes are affected (approximately 15 per cent) is unusual among the osteogenic sarcomas as a group, and suggests a lower evolutionary form of osteogenesis for this tumor. The extremely malignant clinical course also implies a primitive tissue of origin. These clinical aspects of this neoplasm, the tendency for the tumor to be related to periarticular structures and the rapid clinical course with its usually fatal outcome may be singled out as fundamental characteristics of the growth.

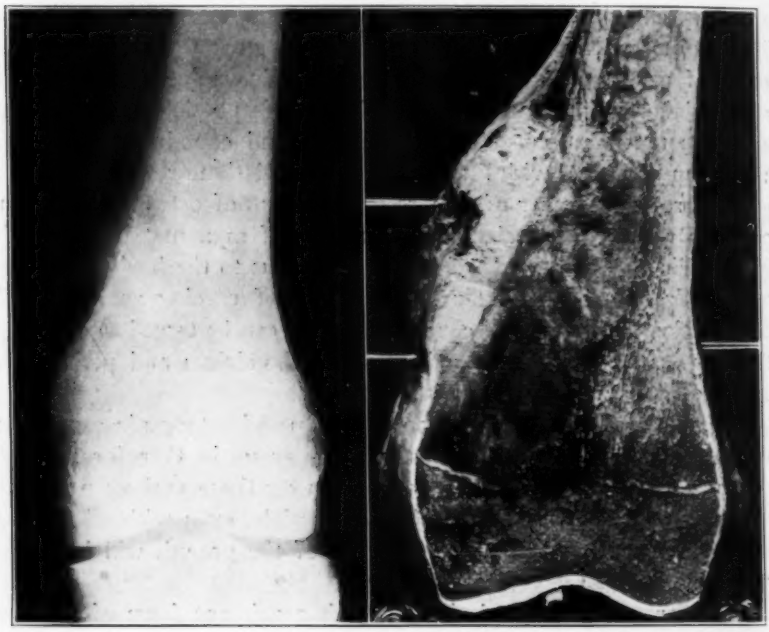

Fig. 40 (P. N. 42358).—Roentgenogram and gross specimen of a primary chondromyxosarcoma. The patient was a white boy, aged 18, with an onset of symptoms one month previously of pain and tumor in the medial aspect of the lower end of the femur. The lesion was explored, and amputation done. The patient died nine months later. The roentgenogram, shows a translucent periosteal shadow above the internal condyle of the femur, with definite periosteal lipping above and radiating spicules (probably calcified) next to the bone. The gross specimen shows more definitely the actual size and location of the tumor mass, emphasizing the translucent character in the roentgenogram of most of the tumor substance.

These primarily malignant tumors occur in patients under 30, sarcoma of this form appearing as an initial lesion most frequently in patients from 14 to 21 years, in the postadolescent period (table 4 and

fig. 41). The youngest patient in this series affected with a primary chondrosarcoma was 6 years, the oldest 45.

The favorite sites for these lesions are about the knee and at the shoulder and pelvic girdles (fig. 42). The majority are about the knee in the lower end of the femur or upper end of the tibia, forty-six of seventy-nine of the neoplasms in this series being located at these points. In the lower end of the femur the line of insertion of the adductor magnus along the linea aspera and at the adductor tubercle on the medial condyle is the predominant focus. The point of origin of the lateral

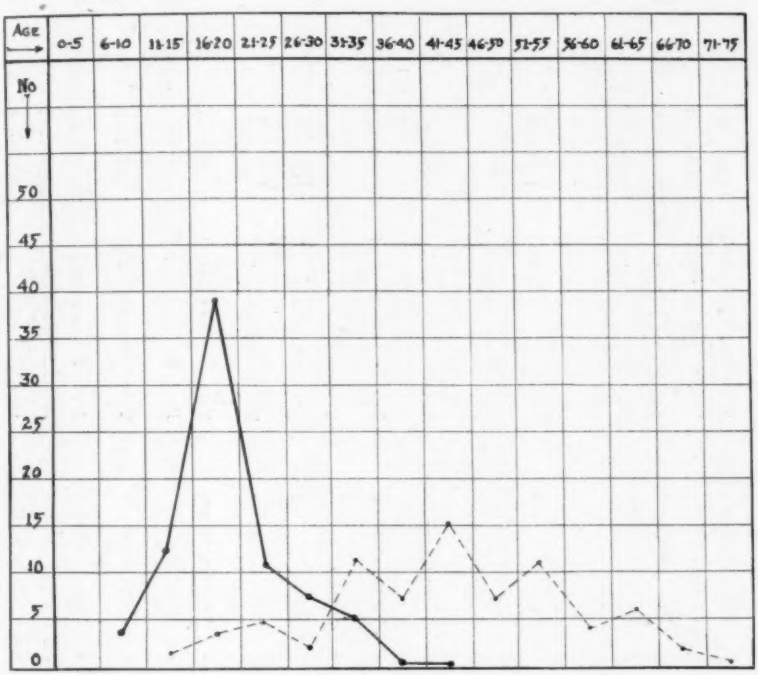

Fig. 41.—Chart showing age incidence among cases of primary chondromyxosarcoma. The solid line indicates the curve in seventy-nine cases of primary chondromyxosarcoma; the broken line, in seventy-five cases of secondary chondromyxosarcoma.

head of the gastrocnemius at the lateral femoral condyle is also occasionally involved. In the upper end of the tibia, the insertion of the quadriceps tendon at the tibial tuberosity is most frequently affected.

The distribution of these lesions shows a relationship to points of muscular attachment and to articular regions where cartilage formation persists throughout life. These sites of muscle attachment are, as has been seen, those of the long muscles exerting a maximal traction, such

TABLE 4.—*Primary Chondromyxosarcoma*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment
43820	W	M	34	Femur, lower	10	Pain; swelling	Translucent periosteal shadow	Amputation	Chondromyxosarcoma	Well 2 mo.
43610	W	F	18	Femur, lower	2	Pain; swelling	Translucent periosteal shadow	Irradiation	.....	Living 1 yr.
42904	W	F	10	Femur, lower	7	Pain; swelling	Periosteal shadow, bone destruction	Curettement; amputation	Chondromyxosarcoma	Discharged well
42894	W	F	24	Humerus, right upper	2	Pain; swelling	Periosteal shadow, bone destruction	Biopsy; irradiation; amputation	Chondromyxosarcoma	Discharged well
42358	W	M	18	Femur, lower, medial	1	Tumor; pain	Translucent periosteal shadow; slight bone destruction beneath	Exploration; amputation	Chondromyxosarcoma*	Dead 9 mo. later†
42356	W	M	19	Femur, lower	2	Trauma	Translucent periosteal shadow; some radiating new bone	Exploration; amputation	Chondromyxosarcoma	Discharged well
42352	W	M	20	Tibia, lower	5	Trauma; pain; tumor	Translucent periosteal shadow at tuberosity	Amputation	Chondromyxosarcoma	Discharged well
42350	W	M	17	Femur, lower; internal condyle	5	Pain; tumor	Translucent periosteal shadow; slight bone destruction beneath	Amputation	Chondromyxosarcoma	Discharged well
42348	W	F	20	Tibia, upper	9	Pain; tumor	Translucent periosteal shadow; some radiating new bone	Exploration; excision; radium	Chondromyxosarcoma	Living 20 mo. after first operation
42346	W	F	13	Tibia, shaft	8	Trauma; tumor	Translucent periosteal shadow; some radiating new bone	Amputation	Chondromyxosarcoma	Well 3 yr.
42344	W	F	12	Femur, lower	2	Tumor	Translucent periosteal shadow; some radiating new bone	Erysipelas and prodigiosus toxins (Coley's)	.....	Dead 7 mo. later
42342	W	M	18	Femur, upper	5	Tumor; pain	Translucent periosteal shadow	Exploration; amputation	Chondromyxosarcoma	Dead 11 mo. later
42228	W	M	23	Femur, upper, middle	2	Pain, 2 months; swelling, 1 week	Translucent periosteal mass; right angle new bone	Roentgen therapy	.....	Living 6 mo. later
42178	W	M	15	Tibia, upper	5	Trauma; tumor	Translucent periosteal shadow at tuberosity	Irradiation	.....	Living 2 mo. later
41842	W	F	11	Astragulus, left	1½	Pain; swelling	Periosteal roughening	Curetted; amputation advised but not done	Chondromyxosarcoma	Recurred
41562	W	M	16	Humerus, upper, left	..	Pain; tumor	Translucent periosteal shadow; radiating bone	Irradiation	.....	Dead 6 mo. later
41502	W	M	44	Jaw, left, lower	4	Pain; teeth extracted; tumor	Area of bone destruction	Radium; excision	Chondromyxosarcoma	Living 6 mo.
41410	W	F	16	Fibula, right, upper	2½	Tumor	Destruction with periosteal roughening	Amputation	Chondromyxosarcoma	Dead 6 mo. later
41122	W	F	17	Tibia, upper	4½	Pain; swelling	Periosteal bone destruction and bone formation	Amputation	Chondromyxosarcoma	Well 10 mo. later
41092	W	M	6	Femur, upper	..	Tumor	Translucent periosteal shadow	Roentgen therapy	Chondromyxosarcoma	Well 10 mo. later

41016	W	F	16	Femur, lower	4	Pain; tumor; limp	Translucent periosteal shadow; bone destruction beneath	Amputation	Chondromyxosarcoma	Well 16 mo. later
41006	W	F	15	Femur, lower	..	Tumor	Translucent periosteal shadow; bone destruction beneath	Curetted; amputation later	Chondromyxosarcoma	Dead 6 mo. after amputation
40718	W	M	22	Tibia, head	..	Tumor	.....	Amputation	Chondromyxosarcoma	Dead 8 mo. later; metastasis to chest and skull
40690	W	M	39	Humerus	1	Pain; stiffness	Translucent periosteal shadow; slight bone destruction beneath	Resection	Chondromyxosarcoma	Well 18 mo. later
40564	W	M	15	Tibia, upper	2	Pain; tumor	.....	Amputation	Chondromyxosarcoma	Cachexia 11 mo. later
40494	W	M	32	Second rib and clavicle	6	Pain; tumor	.....	Erysipelas and prodigiosus toxins (Coley's)	.....	Dead 4 mo.
40484	W	M	12	Femur, lower	..	Pain	Translucent periosteal shadow; expansion and destruction	Roentgen therapy	.....	Well 1 yr.
40350	W	F	16	Eleventh rib	3	Tumor	Expansion and destruction	Roentgen therapy and radium	.....	.....
39794	W	M	15	Femur, lower	½	Tumor; pain	Translucent periosteal shadow; radiating new bone	Amputation	Chondromyxosarcoma	Dead 11 mo. later
39724	W	M	14	Pubis	..	.....	Periosteal new bone	Roentgen therapy	.....	Well 29 mo. later
39180	W	M	12	Humerus, shaft	12	Tumor	Translucent periosteal shadow	Irradiation	.....	Living 9 mo.
39140	W	M	9	Femur, lower	1	Pain; tumor	.....	Exploration	Chondromyxosarcoma	Well 3 yr. later
38814	W	M	18	Femur, lower	6	Tumor	Periosteal translucent shadow	Excision	Chondromyxosarcoma	Recurred 6 mo. later
38620	W	F	15	Tibia, upper	6	Trauma; pain; tumor	Periosteal translucent shadow	Amputation	Chondromyxosarcoma	Well 4 mo. later
38566	W	M	..	Femur, shaft	..	Tumor; pain	.....	Amputation	Chondromyxosarcoma	Dead 2 yr. later
38410	W	M	45	Jaw, lower	7	Pain; abscess	Bone destruction	Drainage and excision	Chondromyxosarcoma	Dead 2 yr. later
37930	W	M	18	Femur, lower	2	Trauma; pain	Translucent periosteal shadow	Irradiation; amputation	Chondromyxosarcoma	Dead 1 yr. later
37324	W	M	14	Tibia, upper	9	Pain; tumor	Translucent periosteal shadow	Roentgen therapy	.....	Dead
36620	W	M	34	Humerus, shaft	..	Tumor	Translucent periosteal shadow	Irradiation; amputation	.....	Dead 6 mo. later
36484	W	F	9	Tibia, upper	6	Trauma; pain; limp	Translucent periosteal shadow	Exploration; amputation; toxins	Chondromyxosarcoma	Dead 6 mo. later
35532	W	M	15	Femur, lower	2	Pain; tumor	Translucent periosteal shadow; radiating new bone	Irradiation; amputation	Chondromyxosarcoma	Dead 18 mo. later

* The term chondromyxosarcoma indicates a microscopic picture comprising: myxoma, fetal, adult and calcifying cartilage and occasional new bone formation.
† The results given show the duration calculated from the date of treatment. The duration of symptoms is from the subjective onset.

TABLE 4.—*Primary Chondromyxosarcoma—Continued*

Pathologic No.	Race	Sex	Age	Location	Duration, Mo.	Symptoms	Roentgenographic Appearance	Treatment	Microscopic Changes	Results of Treatment
35010	W	M	23	Radius, shaft	3	Pain	Translucent periosteal shadow	Curettement	....	.....
34084	W	M	26	Tibia, upper	..	Pain	Translucent periosteal shadow; bone destruction	Amputation; irradiation	....	Dead 1 yr. later
34056	W	M	17	Humerus, upper	27	Trauma; tumor	Translucent periosteal shadow	Roentgen therapy and serum	.....	Dead 2 yr. later
33035	W	F	16	Humerus, upper	2	Trauma; pain; tumor	Translucent shadow of soft part	Irradiation	.....	Dead 3 mo. later
32990	W	M	19	Tibia, upper	10	Pain; tumor	Translucent periosteal shadow; radiating new bone	Amputation	Chondromyxosarcoma	Dead 2 yr. later
32909	W	M	19	Femur, lower	3	Trauma; pain; tumor	Translucent shadow of soft part; bone destruction	Roentgen therapy; toxins; amputation	Chondromyxosarcoma	Well 10 yr. later
32348	W	F	16	Tibia, upper	3	Trauma; pain; tumor	Periosteal shadow; bone destruction	Irradiation; exploration	Chondromyxosarcoma	Dead 1 mo. later
32131	C	M	13	Femur, lower	3	Pain; swelling	Translucent shadow of soft part	Roentgen therapy	.....	Lost
31940	C	F	25	Femur	8	Tumor	Translucent periosteal shadow; radiating new bone and bone destruction	Amputation	Chondromyxosarcoma	.....
31523	W	M	14	Tibia, upper	4	Pain; tumor	Translucent periosteal shadow; radiating new bone	Excision; amputation	Chondromyxosarcoma	Dead 3 yr. later
30880	W	M	33	Iliac crest and pelvis	4	Pain; tumor	Translucent periosteal shadow; bone destruction beneath	Irradiation; toxins	... .	Dead 1 yr. later
30475	C	F	33	Tibia, upper	17	Pain; tumor	Translucent periosteal shadow; bone destruction beneath at tuberosity	Resection; amputation	Chondromyxosarcoma	Lost
29468	C	M	22	Ulna, shaft	1	Pain; tumor	Translucent periosteal shadow; radiating new bone	Amputation	.....	Well 6 yr. after

28801	W	M	19	Femur, lower	2	Pain; tumor	Translucent periosteal shadow; bone destruction beneath	Irradiation; amputation	Chondromyxosarcoma	Dead 2 mo. later
28700	..	F	25	Radius	6	Tumor	.....	Exploration; curettement; roentgen therapy; toxins	Chondromyxosarcoma	Dead
28396	W	F	24	Tibia, upper	6	Tumor; pain	Periosteal translucent shadow	Amputation	Chondromyxosarcoma	Dead 5 yr. later
28239	W	M	18	Femur, lower	4	Pain; tumor	.....	Amputation	Chondromyxosarcoma	Dead 2 yr. later (metastases to liver and intestines)
28057	W	M	16	Femur, lower	1	Trauma; tumor	Translucent periosteal shadow	Amputation; radium	Chondromyxosarcoma	Dead 3 mo. later (metastasis to bone)
27824	W	M	10	Tibia, upper	1	Pain; tumor	Translucent periosteal shadow	Excision	Chondromyxosarcoma	Dead 6 mo. later
27695	C	F	18	Femur, lower	4	Pain; tumor	.....	Amputation; irradiation	Chondromyxosarcoma	Dead 6 mo. later
27581	W	M	22	Femur, lower	2	Pain; tumor	Translucent periosteal shadow	Exploration; amputation	.....	Died, second operation
23637	W	M	..	Femur, lower	..	.....	.....	Excision	Chondromyxosarcoma	.....
21357	W	M	17	Femur, lower	1	Pain	Translucent periosteal shadow; radiating new bone	Amputation	Chondromyxosarcoma	Dead 13 mo. later
20166	W	M	14	Fibula, upper	2	Pain; tumor	Periosteal new bone; bone destruction	Incisions; curettement	Chondromyxosarcoma	Dead 3 yr. later
19419	C	F	15	Femur, lower	3	Pain; swelling	Calcifying periosteal shadow	Amputation	Chondromyxosarcoma	Dead 7 mo. later
17584	C	F	14	Tibia, upper	6	Trauma; tumor	.....	Amputation	Chondromyxosarcoma	Dead 3 yr. later
17525	W	M	20	Femur, lower	3	Trauma; tumor	Translucent periosteal shadow; radiating new bone	Amputation	Chondromyxosarcoma	Dead
16347	W	F	25	Tibia, upper	8	Pain; tumor	Periosteal new bone; bone destruction	Amputation	Chondromyxosarcoma	Dead 15 mo. later
15838	W	M	21	Humerus	5	Pain; tumor	.....	Amputation	Chondromyxosarcoma	Dead 13 mo. later
15557	W	M	21	Femur, lower	2	Pain; tumor	Periosteal new bone; bone destruction	Amputation	Chondromyxosarcoma	Dead 2 yr. later
11670	W	M	17	Tibia, upper	8	Pain; tumor	Translucent periosteal shadow; bone destruction beneath	Amputation	Chondromyxosarcoma	Dead 1 yr. later
8066	W	M	17	Sacrum, upper	12	Trauma; tumor; paraplegia	.....	Exploration	Chondromyxosarcoma	Dead 1 yr. later
2331	W	M	17	Vertebra, lower lumbar	12	Trauma; pain	.....	Exploration	Chondromyxosarcoma	Dead 1 yr. later
1890	W	F	22	Ischium	48	Trauma; pain	.....	Partial excision	Chondromyxosarcoma	Recurrence 3 mo. later, dead 1 yr.

as the rectus abdominus, the quadriceps femoris, the adductor magnus and the gastrocnemius. As in the exostoses, the points of origin for this type of tumor show an anatomic peculiarity in the periosteum. Here the normal fibrous layers of the periosteum are interrupted to allow osseous fusion with the end of a tendon, and at the point of fusion, precartilaginous tissue, from which such structures as the adductor tubercle or the tuberosity of the tibia are formed, persists both beneath the periosteum and within the substance of the tendon.

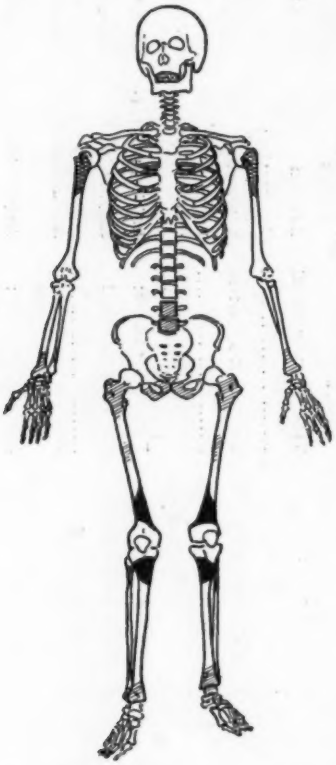

Fig. 42.—Incidence of primary chondromyxosarcomas according to skeletal location. The solid black areas indicate the most frequent sites; the checked areas, the common sites, and the diagonal lines, the occasional or rare locations.

The symptoms related by a patient suffering from this primary form of chondrosarcoma are confined to a period of about five months and begin with a complaint of pain, which may or may not follow a relatively mild form of trauma. The pain becomes rapidly more constant and severe and soon interferes with the function of the part. Since the region of the knee is usually involved, the stiffness of this joint, with the assumption of a position of partial flexion is a common condi-

tion. Weight-bearing in the affected leg soon becomes painful, and limping is followed by the use of crutches, full relief soon being impossible even when the painful region is put at complete rest.

Examination reveals swelling in the region of the flexed joint and a tumor with a rubbery consistency that is larger to palpation than the x-ray films would seem to indicate. Pathologic fracture is exceedingly rare because of the acute course and the periosteal nature of the lesion. Among the constitutional manifestations of primary chondrosarcomas, fever, leukocytosis and an enlargement of the regional lymph nodes are occasionally observed. The glandular enlargement is noted only in association with fever, and, to my knowledge, metastases to these glands have not been demonstrated by histologic examination, although such secondary growths in other forms of osteogenic sarcoma have been recorded in rare instances in this laboratory. These systemic reactions as well as a secondary anemia are late manifestations of the disease and should play no part in making the diagnosis.

ROENTGENOGRAPHIC FEATURES

Three important features are typical of the x-ray picture of primary chondrosarcoma. These are the faintly visible and fairly translucent shadow of the soft part next to the bone, the raising of the adjacent periosteum and the frequent absence of cortical or medullary involvement of the bone. The entire tumor is outside of the bone proper in early cases, and because its cartilaginous substance casts so little shadow on the film, this may well be considered the invisible tumor of the bone which is in danger of being overlooked or misdiagnosed by those unfamiliar with this early roentgenographic picture. When new bone or calcification of tumor origin is present, it is always sparse and has a tendency to take the form of finely radiating lines at right angles to the cortex (fig. 43). Unlike the "sun ray" or sclerosing type of osteogenic sarcoma, dense shaggy lines of periosteal new bone are lacking. This type of sarcoma also differs from the sclerosing form in that it is less likely to involve the marrow cavity, and when doing so late in the disease produces bone destruction in the medulla rather than areas of increased density as in the sclerosing form (Geschickter [15]).

This primary form of chondrosarcoma is to be distinguished from the benign osteochondromas in the roentgenogram, by its more faintly visible tumor shadow, by its more indefinite and infiltrating outward margin and also by the failure of the cortex beneath the tumor to form a base or pedicle for the growth as it does in exostoses. When such a chondromyxosarcoma arises as a secondary malignant change in a benign exostosis, this sarcomatous transformation in the benign tumor is evident in the roentgenogram by the blurring and blotting out of the

distinguishing lines differentiating cancellous from cortical bone in the base of the exostosis, and the whole tumor soon becomes a blurred and granulated mass (fig. 44). These secondary chondrosarcomas are discussed separately in more detail below.

The early stage of myositis ossificans may be mimicked (Lewis [16]) in appearance by the delicate lines of ossification in this form of chondrosarcoma, but in the sarcoma the outer border of the tumor never has the definite edge seen in myositis ossificans, and the laminated bony structure paralleling the shaft of the bone is absent. The favorite

Fig. 43 (P. N. 39114).—Roentgenographic appearance of the primary chondromyxosarcoma in which early signs of calcification and ossification are present in the tumor area next to the bone. Note the faintly visible periosteal shadow, the absence of cortical or medullary involvement in the bone and the location at the site of the adductor tubicle.

location of myositis ossificans in the adductor muscles of the thigh and the branchialis anticus of the elbow is not a common site of this form of osteogenic sarcoma, nor is there the same definite relationship to a trauma preceding the lesion by a period of from four to six weeks (fig. 9).

16. Lewis, D.: Myositis Ossificans, J. A. M. A. **80**:1281 (May 5) 1923.

GROSS PATHOLOGY

Biopsy of these tumors reveals, beneath a raised and perforated periosteum, a pearly gray and shiny substance of varying consistency, some of it is well formed cartilage, other parts cystic and hemorrhagic. The various lobules that compose the tumor show a tendency to extend lengthwise up and down the bone and around it, rather than to invade the marrow cavity. However, in advanced cases, the cortex is broken through, and neoplastic tissue infiltrates the medulla of the bone. It is such advanced cases with involvement of the marrow cavity by cartilaginous tumor substance that are most common in the older literature, and for this reason there has been an erroneous conception that this type of tumor is of central rather than of periosteal origin (fig. 45).

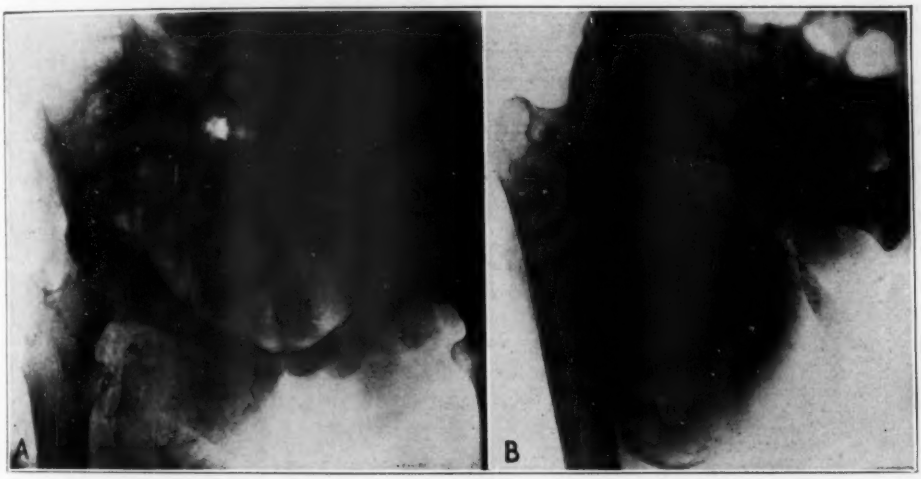

Fig. 44 (P. N. 32485).—Roentgenogram of a case of secondary chondromyxosarcoma arising in a benign osteochondroma. *A* shows the osteochondroma arising in the lower ramus of the pubic bone. *B* shows the same lesion three years later with definite malignant change. Note the granular character of the neoplasm, its immense size and the fracturing of the pubis and the ischium. The patient was a white woman, aged 30, who had known of the presence of the tumor for over three years. Deep roentgen therapy was administered, but the patient died of internal metastases five years after the treatment was begun.

Small pockets that exude a sanguineous synovial-like fluid are not rare in these growths. Such cystic areas containing what is a pseudo-joint fluid make the exploration of these neoplasms by one unfamiliar with their pathology an extremely dangerous procedure. Myxomatous tissue contained in the outpouring fluid is the mother substance of these tumors, and is even more readily transplanted than is the myxoma of the benign chondroma (fig. 46).

One of the striking features of the tumor growth is the metastasis or gradual extension into the large veins. H. J. B. Fry [17] reported a case in which the tumor arising from the sacrum metastasized to the inferior vena cava and completely filled the right side of the heart with a soft cartilaginous mass. Phemister [18] reported a similar case in which the cartilaginous growth filled the femoral vein by direct extension from a tumor arising in the femur.

In occasional gross specimens, the early lobules of the tumor may be seen sprouting from fibrous strands of a tendon such as the quadriceps

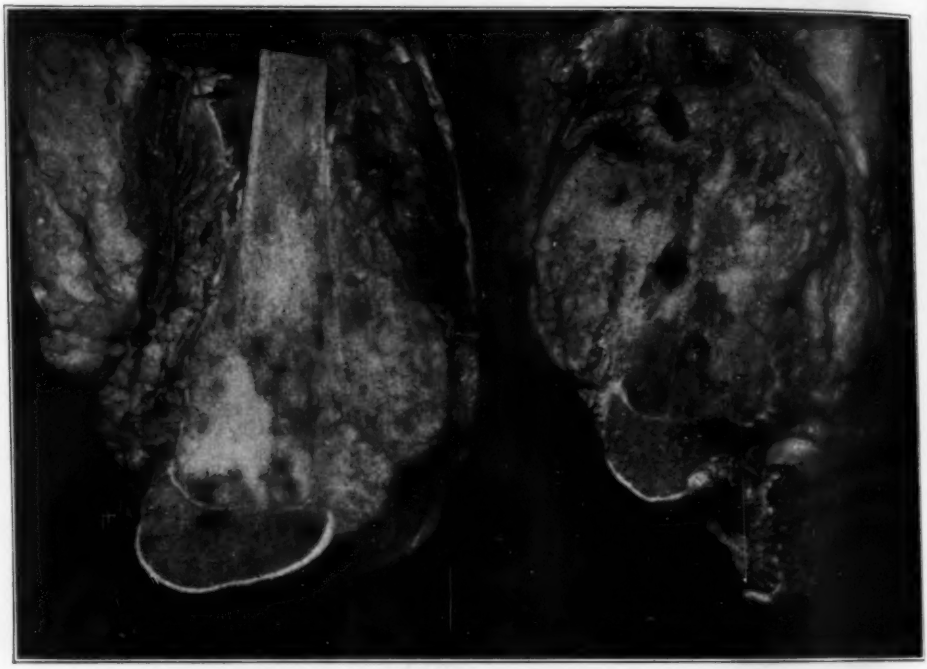

Fig. 45 (P. N. 19419).—Specimen of a primary chondrosarcoma in the lower end of the femur of a colored girl, aged 15. The periosteal tumor has invaded the marrow cavity, producing a dark cystic area shown in the right hand specimen. The clinical course was extremely brief, slightly over three months of symptoms and death within seven months after the primary amputation.

in the region where it envelopes the patella or the attachment of the adductor magnus at the line of insertion at the adductor tubercle. This relationship is particularly striking in some cases and may be verified

17. Fry, H. J. B., and Shattock, C. E.: Chondrosarcomatous Permeation of the Inferior Vena Cava and Right Side of the Heart, Brit. J. Surg. **14**:337, 1926.

18. Phemister, D. B.: Chondrosarcoma of Bone, Surg. Gynec. Obst. **50**:216 (Jan.) 1930.

microscopically by sections from properly chosen areas (fig. 47). Frequently, however, the tumor has extended sufficiently to obscure its mode of origin, and no definite conclusions can be drawn from the specimen.

MICROSCOPIC OBSERVATIONS

The analysis of microscopic sections of a series of cases of primary chondrosarcoma is essentially a study in miniature of the entire embryology of bone. Here the very earliest stages of cartilage formation from connective tissues can be found as well as the advanced calcifying

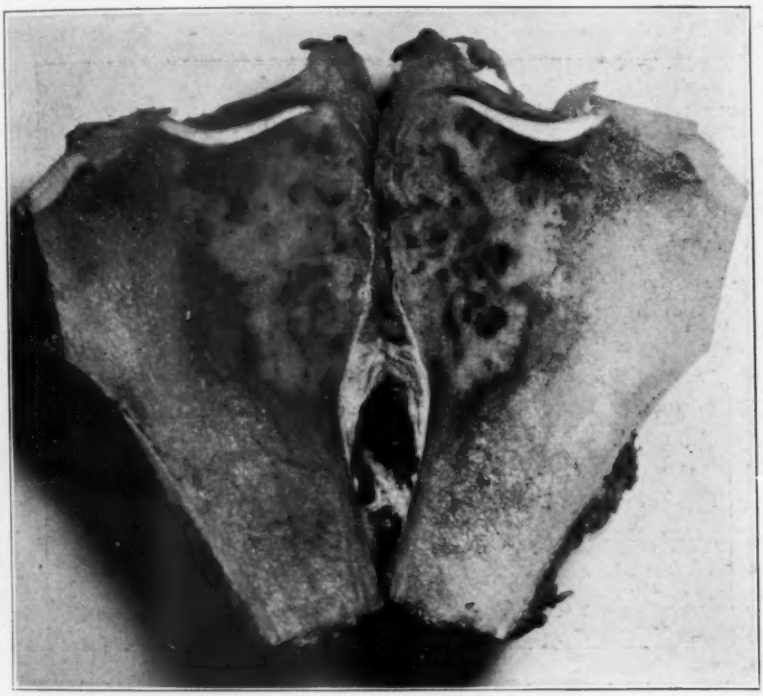

Fig. 46 (P. N. 41122).—Cysts in the chondromatous tissue of a primary chondrosarcoma occurring at the site of the tibial tuberosity. The patient was a white girl, aged 17, who complained of pain and swelling of four and a half months' duration. She has remained well ten months following a primary amputation.

forms. In addition, but less frequently, the phase of substitution bone which follows in the wake of calcified cartilage can be seen in the form of ossification proceeding from early connective tissue. At other times, although rarely, an intervening resorptive stage characterized by giant cell proliferation occurring before calcified cartilage is replaced by bone, can be found in the more slowly growing areas of these tumors. This rehearsal of the entire embryology of normal bone in distorted and abortive form by chondromyxosarcoma is explicable only on the basis

that the tissue of origin of this tumor represents the earliest type of undifferentiated connective tissue concerned with ossification. At this primitive stage, this tissue has the full potentialities of subsequent differentiation essential for all of the various structures of the future skeleton. Embryologically, such a tissue is best represented by the perichondrium which although primarily concerned with the proliferation of cartilage, subsequently differentiates into periosteum and develops the property of direct membranous bone formation. As previously explained, this perichondrium is closely allied or identified with the other types of precartilaginous connective tissue concerned with articular and periarticular functions.

Fig. 47 (P. N. 27695).—Photomicrograph showing the embryonic connective tissue and fetal cartilage cells of a primary chondromyxosarcoma arising from the ends of the tendon. The patient was a colored girl, aged 18, who complained of pain and tumor in the lower end of the femur of four months' duration. She died six months after a primary amputation followed by irradiation.

The fundamental basis of the pathologic process of primary chondromyxosarcoma is to be found under the microscope in nearly all of the sections taken from this type of tumor. Histologically, the growth arises from a dense condensation of embryo-like connective tissue. The cells of this tissue, which are either stellate or an elongated spindle shape, give origin to a syncytium (fig. 48) with an increasing amount of clear, hyaline-like ground substance, in which the connective tissue

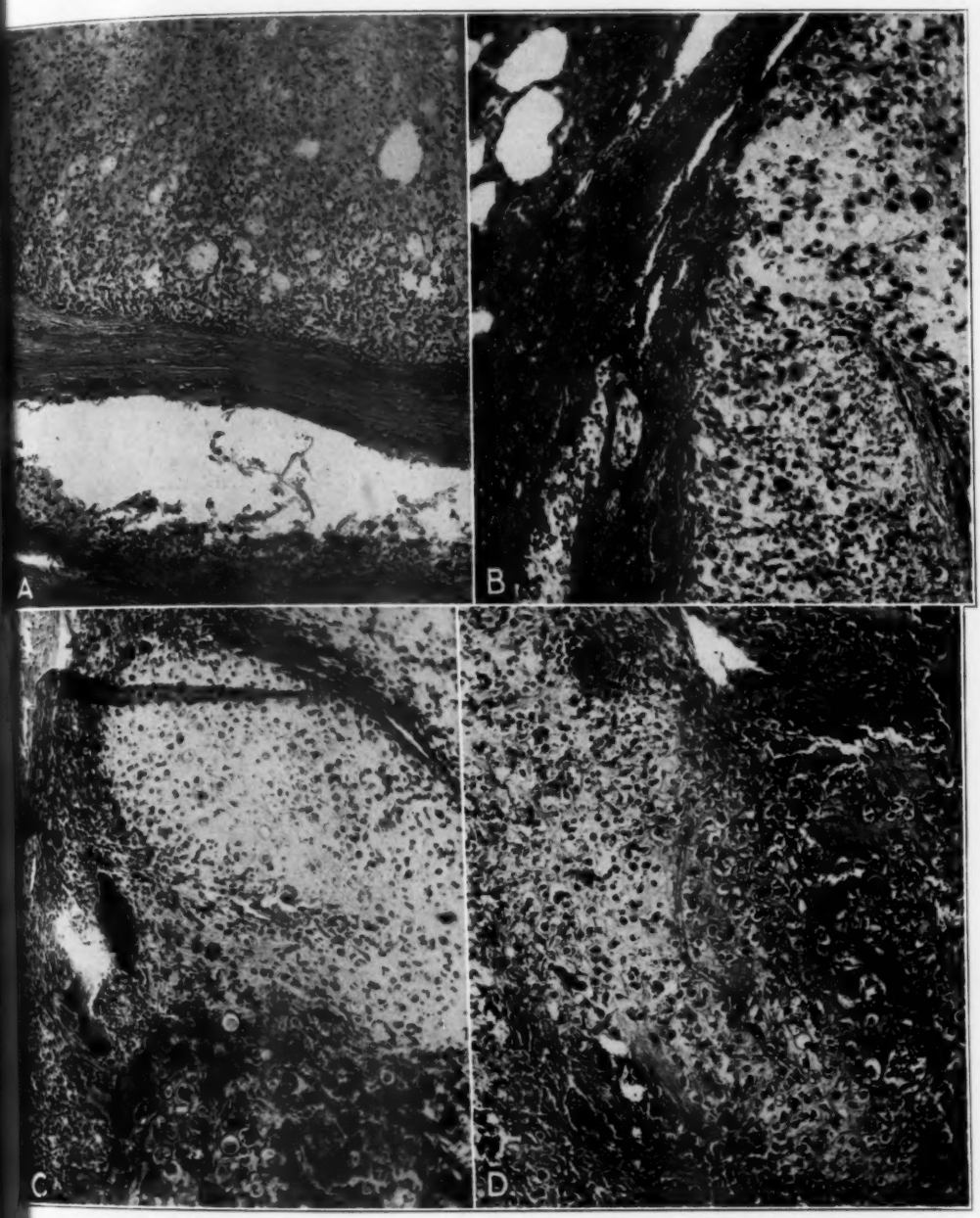

Fig. 48.—Studies showing the cycle of tissue differentiation in chondromyxosarcoma. *A* shows primitive connective tissue and fetal cartilage cells arising from a tendon adjoining the tumor. This is the myxomatous stage. *B* is from a metastatic lung nodule in a case of chondromyxosarcoma and shows the more adult cartilage cells developing in a myxomatous matrix. *C* shows the margin of the tumor in a case of chondromyxosarcoma in which the primitive precartilaginous connective tissue is giving rise to adult and calcifying cartilage. This is the cartilaginous stage. *D* is from the central portion of a chondromyxosarcoma and shows the primitive connective tissue in the tumor giving rise to direct bone formation of neoplastic origin.

cells after assuming a rounded form, become embedded. This syncytial tissue is typical myxoma, and the scattered rounded cells with small dense nuclei and clear, deeply acidophilic cytoplasm are fetal cartilage cells. Later these cells surround themselves with small lacunae, which gradually take a definite capsular form, abutting on the ground substance in a fashion that duplicates typical adult hyaline cartilage. This adult cartilage differs from that found at the normal epiphyseal line and in benign chondromas and osteochondromas in that the cells show less tendency to arrange themselves in definite columns and, in addition, contain nuclei that are larger, more vesicular and more frequently undergoing mitosis. Fibrous septums dividing the cartilage into lobules are also more frequent and far more cellular in these malignant growths, and calcification occurs more sporadically and irregularly.

This transition from fibrous tissue to cartilage with an intermediate syncytial or myxomatous stage (fig. 49) has been responsible for the connotation of chondromyxosarcoma given to this tumor. Contrary to the traditional views of Ribbert,[19] Sternberg,[20] Kolodny,[21] and others, the myxomatous substance in these lesions is not a product of cartilaginous degeneration but the predecessor of the later chondral forms which are derived from it, a view that is fully substantiated by the studies herein presented and with which Borst [22] is in full accord. The fact that mucoid cysts and pockets of syrupy synovial-like fluid are to be found in association with these myxomatous areas is not a phenomenon of degeneration but concerns the embryologic rôle which this tissue plays in the formation of normal joint cavities.

Bone formation is not prominent in these primary chondrosarcomas. When found, the osseous tissue is usually next to the periosteum overlying the tumor and is either reactive bone, proceeding from normal periosteum, or ossification of tumor origin arising in the dense embryonal connective tissue strands dipping from the capsular margin into the tumor substance (fig. 50). The fact that the latter type of bone, thus produced, is neoplastic in origin and not reactive is substantiated by the finding of similar areas in metastatic nodules of the lung (figs. 51 and 52). This neoplastic ossification is always sparse in primary chondromyxosarcoma, but when it does occur it must be taken as an indication that the primitive perichondrium or precartilaginous connective tissue from which these growths arise is differentiating in two directions, one toward the proliferation of cartilage and the other a trans-

19. Ribbert, H.: Geschwulstlehre für Aerzte und Studierende, Bonn, F. Cohen, 1904.

20. Sternberg, K.: Personal interview with the author, July, 1929.

21. Kolodny, A.: Bone Sarcoma: The Primary Malignant Tumors of Bone and the Giant Cell Tumor, Surgical Publishing Company of Chicago, 1927.

22. Borst, M.: Personal interview with the author, July, 1929.

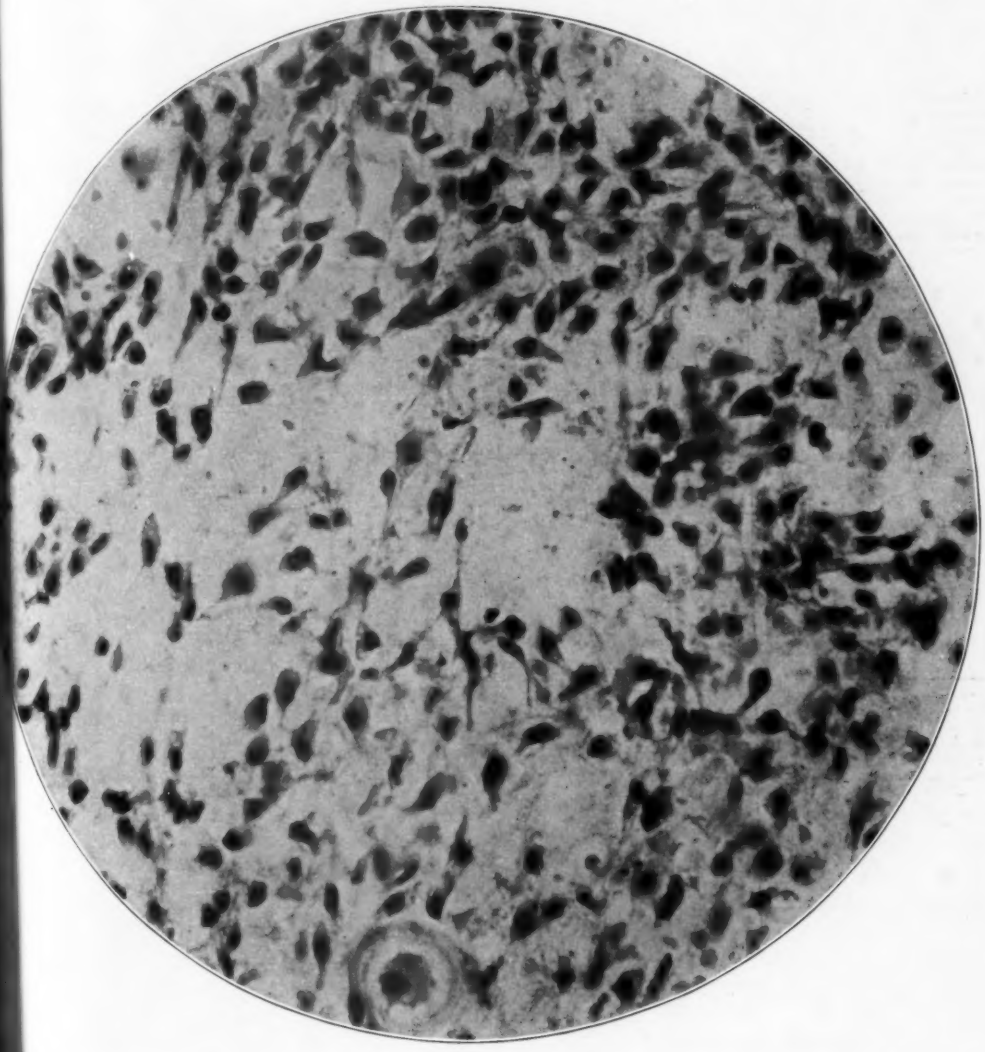

Fig. 49 (P. N. 27695).—High powered photomicrograph of the lesion depicted in figure 47. This illustrates clearly the differentiation of fetal cartilage cells from the spindle cells forming the so-called myxoma. In the lower part of the picture there is shown an early cartilage cell secreting a capsule about itself. The cartilaginous tissue in this case is clearly proliferated from the preceding myxomatous state, contrary to the traditional views that the myxomatous tissue is a degenerate product of cartilage.

formation toward adult periosteum with the production of direct membranous bone.

From a diagnostic standpoint, it is sometimes extremely difficult to be certain of the presence of chondromyxosarcoma under the microscope and to distinguish these lesions from the more cellular types of benign chondromyxoma. In a review of many sections, the cellular nature of the connective tissue strands, the presence of myxoma and fetal cartilage, the malignant nuclei of the cartilage cells and the occasional presence of cellular areas containing round cells midway between fetal cartilage

Fig. 50 (P. N. 32990).—Photomicrograph showing a primary chondromyxosarcoma. The patient was a white man, aged 19, with symptoms of pain and swelling of ten months' duration in the upper end of the tibia. The roentgenogram showed a translucent periosteal shadow with a few radiating spicules of new bone. Amputation was performed June, 1923. The patient died with metastasis to the lungs two and one-half years later, in 1926. The photomicrograph shows the periosteal border of the tumor. There is a proliferation of dense embryonic connective tissue with the formation of a hyaline matrix containing fetal and adult cartilage cells. The lower right hand corner shows calcifying adult cartilage. The small amount of new bone near the tumor capsule is proceeding from primitive connective tissue.

and chondroblasts in differentiation (fig. 53) have been found helpful in identifying chondromyxosarcoma.

HISTOGENESIS

From the standpoint of histogenesis, it is evident that this form of chondrosarcoma is related by location and by histology to primitive precartilaginous tissue. Its occurrence at the sites where tendons attach directly to bone and participate in the formation of normal bony protuberances for the anchoring of such tendons shows that the developmental steps from connective tissues to cartilage to bone persist normally in these regions. Adequate evidence to substantiate such a

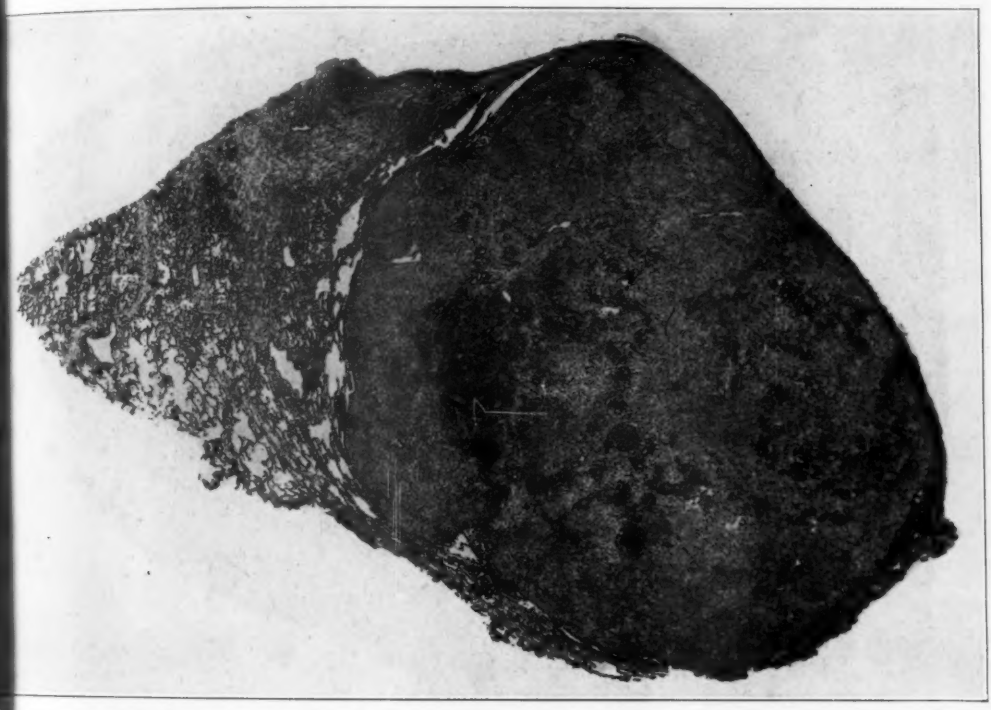

Fig. 51 (P. N. 31523).—Low powered photomicrograph of a metastatic nodule in the lungs of a patient dying of chondromyxosarcoma.

conclusion has been presented in tracing the histogenesis of the benign exostoses (see page 245, section marked Histogenesis).

The presence of this relatively undifferentiated fibrous tissue which retains such embryonic functions at the sites where chondromyxosarcomas arise does not necessarily represent fetal cell rests in the sense of Cohnheim.[23] The evidence educed here favors the view that the persistence of this tissue about periarticular points provides a normal

23. Cohnheim, J.: Vorlesungen über Allgemeine Pathologie Ein Handbuch für Aerzte und Studierende, Berlin, 1877-1880.

growth center which functions in maintaining tendon length in keeping with increased skeletal growth. This would account for the origin of these primary forms of ossifying chondrosarcoma during the age period of maximum skeletal growth, and would indicate that the normal

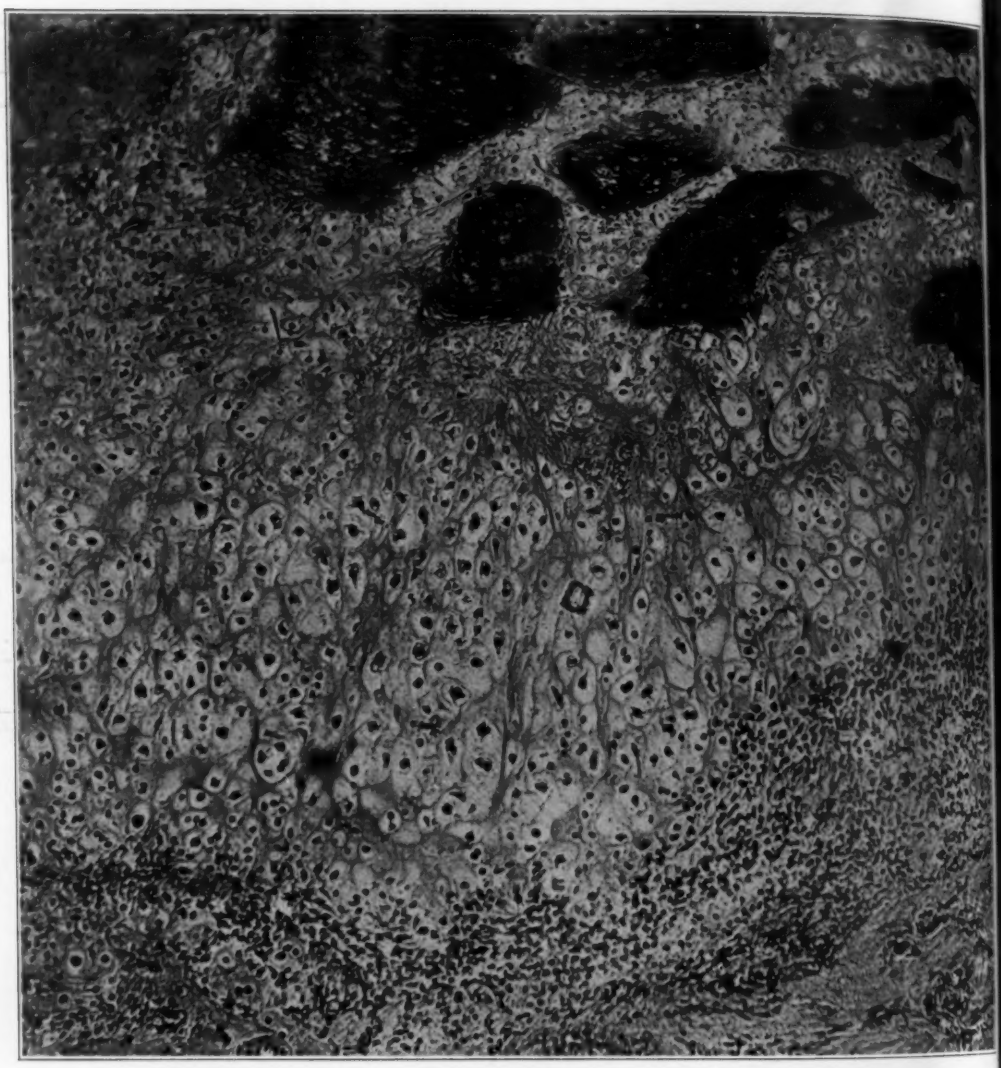

Fig. 52 (P. N. 31523).—Higher magnification of lung nodule shown in figure 51. The new bone depicted in the high power illustration shows clearly the power of bone formation residing in the primitive connective tissue found in this form of neoplasm.

cytologic transitions accompanying tendon growth form a fundamental basis for the origin of this tumor. This conclusion that both normal

growth impetus and a normal cycle of histogenic differentiation at a growth center is essential to the inception of this form of sarcoma of bone is substantiated by the study of the other types of osteogenic sarcoma which arise under similar circumstances.

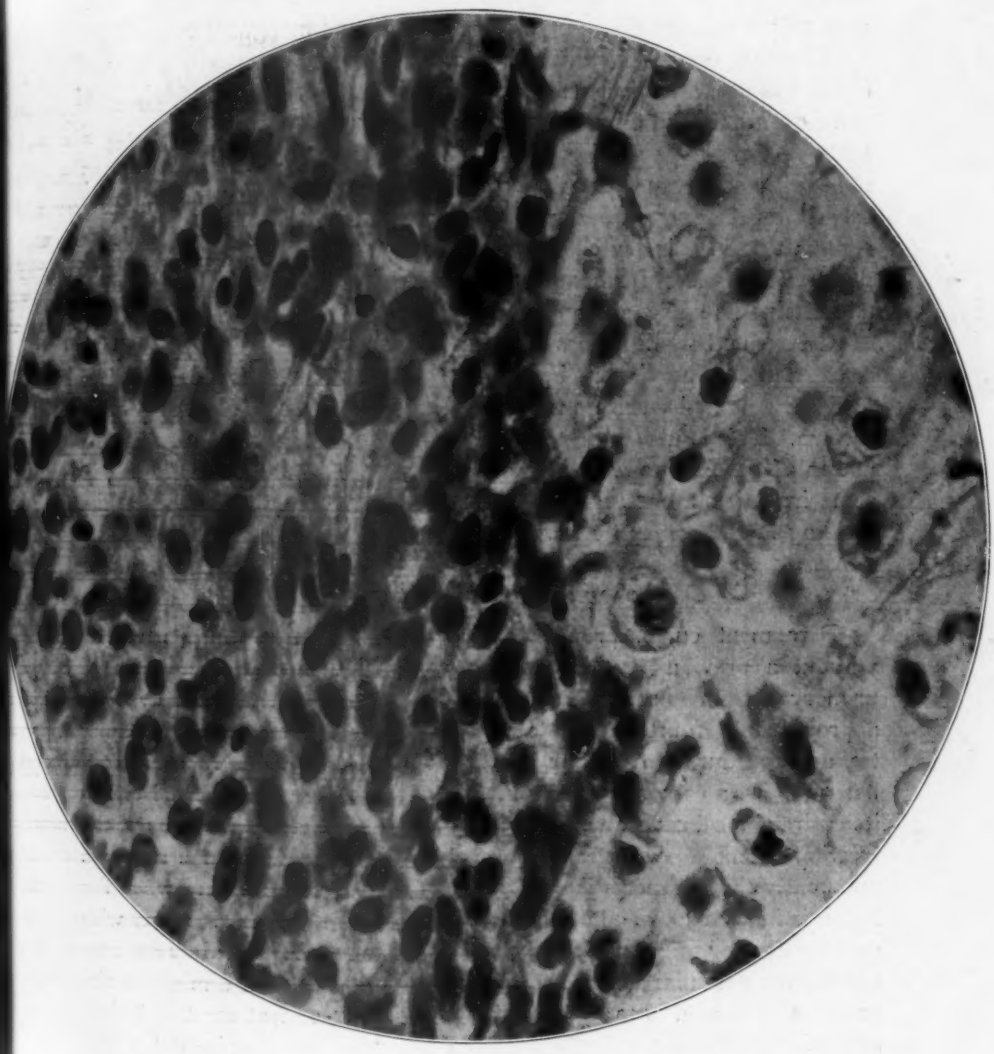

Fig. 53 (P. N. 20116).—Photomicrograph showing the cellular areas containing round cells midway between fetal and adult cartilage, characteristic of chondromyxosarcoma as distinguished from the benign chondroma.

The close similarity between the mode of origin of the benign exostoses and the primary chondromyxosarcomas raises the question concerning the factors which determine whether a given neoplasm will

pursue a benign or malignant course. For it is fairly certain that at their inception the developmental state of the mother tissues is practically the same for both benign osteochondromas and the malignant primary chondrosarcomas. Why, therefore, should the exostosis be such a slowly growing and benign affair and the chondromyxosarcoma with the same beginning, pursue such a rapid and malignant course?

The only explanation which comes to mind involves a matter of tissue balance, a subject on which there is little or no information. If one assumes that in exostoses the chondromyxomatous cap which represents the neoplastic portion of the tumor is in balance with the ossification which proceeds from the bone beneath and that the overgrowth is caused by an exaggerated periosteal gap, then it becomes feasible to assume that in primary chondrosarcoma no such balance exists, and the neoplastic chondromyxomatus tissue outstrips the adjacent ossification and attains its malignant properties.

On such a basis it is possible to explain the secondary origin of chondrosarcoma in previously benign osteochondromas. These secondary malignant growths arise when a previously existing balance is overthrown. This is usually in the adult when the adjacent bone has lost its power of ossification with increasing age, or in youth when trauma or some irritating agent acts to stimulate unduly, the growth propensities residing in the neoplastic tissue.

PROGNOSIS AND TREATMENT

Permanent cures, even when amputation is performed promptly without a previous exploration, are rare in this malignant form of primary chondrosarcoma. In a fatal case the patient usually lives approximately fourteen and one-half months after operation. Since the average duration of symptoms prior to operation is five and one-half months, a case of primary chondrosarcoma can be expected to run its entire clinical course within twenty months. Neither the age nor the location of the growth greatly influences the ultimate results, although apparently the prognosis is somewhat worse for children and when the lesion is in the upper end of the humerus and of the femur. Delay with prolongation of symptoms previous to operation accompanied by destruction of the medullary bone shown in the roentgenogram diminishes the prospect of a cure. Incomplete initial surgical treatment must be looked on unfavorably, but cures have been accomplished despite delay and recurrence after an initial operation.

If there is failure in the operative procedure, primary chondrosarcoma shows a marked tendency to recur locally as well as to metastasize. The total number of cures in the forty-two cases followed in this series for more than five years was two (table 5). In one case in

which amputation was performed, this procedure followed after radium treatments. In both of these cases microscopic verification of the diagnosis is available in the laboratory.

Deep roentgen therapy, either preceding the operation or given postoperatively, has no influence on the results as far as can be determined from this series of cases. When the patient has refused operation, deep roentgen therapy has apparently been helpful in alleviating pain, except in the more advanced stages of the disease. Its use, however, cannot be considered other than palliative in the dosages ordinarily administered. Radical resection and amputation, when used alone, are rarely successful in accomplishing a cure and should be used in conjunction with a radium pack. In lesions of the skeletal trunk radical excision or resection, followed by thermal cauterization and radium

TABLE 5.—*Results of Treatment in Cases of Primary Chondrosarcoma*

Total number of cases	77*
Lost	4
Total number of cases followed	73
Patients followed less than five years and reported well	18
Patients reported dead since 1925	13
Number of cases followed less than five years	31
Total number of cases followed for more than five years	42
Number of patients living over five years	2
Number of patients dead previous to 1925	40
Percentage of five year cures	5%

* Two recent cases have not been included in this table.

therapy is worthy of a trial. The dosage in such cases must be adequate (15,000 millicurie hours) and competently administered.

SECONDARY CHONDROSARCOMA

In all of the benign tumors of the fibrocartilaginous group, the persistence and functioning of connective tissue of the embryonic precartilaginous type makes possible the origin of secondary chondrosarcoma which is superimposed on the original benign growth.

In many of such secondary lesions evidence of the preexistent growth is easily traced, but in others, in which an obscure and latent defect has been present for many years within the tuberosity of a long bone, urgent symptoms are not manifest until the condition has taken on frankly sarcomatous features.

Attention was first called to the latter type of tumor by Bloodgood [24] in 1906, under the term of pure myxoma of bone. While not con-

24. Bloodgood, J. C.: Bone Tumors, Myxoma, Central and Periosteal, Ann. Surg. **72**:712 (Dec.) 1920.

Fig. 54 (P. N. 6773).—Secondary malignant change occurring in a benign exostosis. The cap of the lesion has been blotted out, and the base of the outgrowth has been invaded by the destructive process of the chondrosarcoma. The patient was a white woman, aged 53, who had had a tender spot and a swelling on the shaft of the left humerus for over twenty years. She had noticed an increase in the lump for only nine months, with increased pain at this site. There was a history of syphilis dating back twenty-six years. This tumor was incised seven times within seven years, the final recurrence necessitating amputation at the shoulder joint. Three years after the amputation and ten years after the first operation, death occurred with metastases to the scalp and mediastinum. The microscopic structure of the tumor is shown in figure 66.

sidered primarily malignant, these lesions usually resulted in death from metastases after repeated recurrences over a period of years. To this clinical entity of Bloodgood, a secondarily malignant origin may now be ascribed on the basis of a restudy of all the cases thus classified by him in the Surgical Pathological Laboratory. These tumors occur most frequently in patients over 30 years of age and in the roentgenogram usually have the structure of a benign chondroma at their base within the bony tubercle but outwardly the translucent and indefinite shadow of a chondromyxosarcoma (fig. 54).

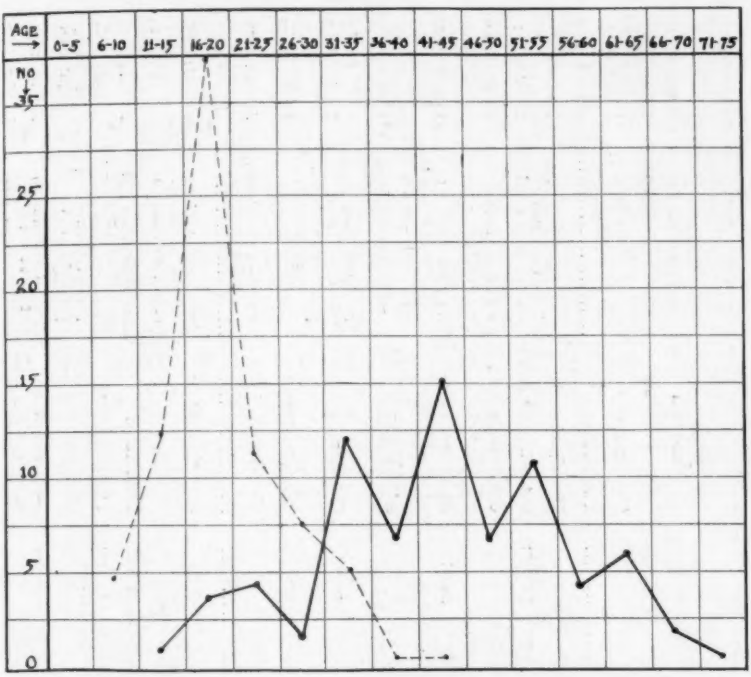

Fig. 55.—Age distribution in cases of secondary chondromyxosarcoma. The broken line shows the incidence in seventy-nine cases of primary chondromyxosarcoma; the solid line, in seventy-five cases of secondary chondromyxosarcoma.

CLINICAL FEATURES

Most of these tumors occur in persons between the ages of 35 and 55 (71 per cent), with the peak of incidence between the ages of 40 and 45. They may, however, occur before the age of 30 (fig. 55). The location of these neoplasms in the skeleton differs from the primary form of chondrosarcoma in that there is a greater tendency for them to occur at the upper end of the humerus, about the ribs and at the heel (fig. 56). The total duration of symptoms in these cases averages over six years in this series, varying from two to twenty-five years.

TABLE 6.—*Secondary Chondromyxosarcoma*

Pathologic No.	Race	Sex	Age	Location	Duration, Yrs.	Symptoms	Primary Condition	Roentgenographic Appearance	Treatment	Microscopic Changes	Result of Treatment
43831	C	F	22	Fibula, upper	4	Tumor; pain	Osteochondroma	Granular periosteal new bone	Resection; irradiation	Chondromyxosarcoma	Discharged well
43255	W	M	35	Femur, greater trochanter	8	Tumor	Chondroma	Trochanter destroyed; medulla rarefied	Excision	Chondromyxosarcoma	.....
43252	W	M	50	Lower end of femur	..	.....	Chondroma	.....	Amputation	Chondromyxosarcoma	.....
42888	W	M	50	Humerus, upper	2	Pain; tumor	Chondromatosis	Bone expansion; new bone formation	Resection	Chondromyxosarcoma	Dead after operation
42390	W	M	50	Pubis, left	25	Trauma; tumor; pain; edema	Osteochondroma	Granular periosteal new bone	Irradiation	.....	Dying
42388	W	M	31	Os calcis; fibula, lower	2	Pain; tumor	Osteochondromas at old fracture site	Large translucent mass about achilles' tendon	Exploration; amputation	Chondromyxosarcoma	Well 5 yr.
42386*	W	M	40	Femur, lower	22	Trauma; pain; tumor	Exostoses; chondromatosis in and about knee joint	Multiple exostoses; joint mice; translucent periosteal shadow	Curettement; amputation	Chondromyxosarcoma	Well 1 yr. later
42382	W	M	47	Rib, third anterior	7	Tumor	Chondroma	Expanded costrochondral junction; translucent periosteal shadow	Resection (3 times)	Chondromyxosarcoma	Three recurrences; dead after 6 yr.
42354	W	M	19	Tibia, upper	..	Tumor, congenital (?); recent pain	Osteochondroma	Pedicle exostoses undergoing destruction and proliferation	Exploration (3 times); amputation	Chondromyxosarcoma	Living 21 mo.
42286	W	M	41	Ischium	..	Tumor; pain	Osteochondroma	Secondary bone destruction in exostosis	Curettement	Chondromyxosarcoma	Recurrence
41558	W	M	35	Humerus, greater tuberosity	5	Tumor	Chondroma	Tuberosity destroyed; acromion rarefied	Amputation	Chondromyxosarcoma	Well 1 yr. later
41103	..	..	..	Ilium, crest	..	.....	.....	.....	Excision	Chondromyxosarcoma	Recurrence
40778	W	M	30	Tibia, upper	2	Pain; tumor; pathologic fracture	Osteochondroma	Translucent periosteal shadow; bone destruction beneath	Curettement (2 times); irradiation; radium and toxins	Chondromyxosarcoma	Recurrence
40642	W	M	15	Metatarsal base, second	2	Tumor; trauma	Chondroma	Central destruction; periosteal roughening	Excision	Chondromyxosarcoma	Dead 1 yr. later
40606	W	M	21	Femur, lower, left; toes right foot	2	Multiple tumors; elephantiasis	Chondroma (?)	Diffuse translucent periosteal shadow; rarefaction of phalanges	Amputation, left leg and right foot	Chondromyxosarcoma	Metastases
40450	W	M	30	Popliteal space	15	Trauma; tumor; pain	Chondromatosis	Translucent shadow of soft spot	Excision	Chondromyxosarcoma	Well 2 mo.
40273	W	F	54	Femur, lower	..	Tumor	Osteochondroma (?)	.....	Exploration	Chondromyxosarcoma	Lost

40154	W	F	62	Scapula, left	½	Tumor; pain	.....	.....	Irradiation; colloidal lead; amputation	Chondromyxosarcoma	Well 2 yr. after operation
39952	C	M	18	Femur, lower, left	3	Trauma; tumor	Osteochondroma	Rounded exostosis; translucent shadow of soft part; new bone	Amputation	Chondromyxosarcoma	Well 8 mo.
38666	W	F	37	Femur, lower, left	1	Trauma; tumor	Chondroma	Translucent periosteal shadow; new bone formation	Excision; amputation	Chondromyxosarcoma	Recurrence; living 2 yr.
37868	W	M	29	Femur, upper	8	Tumor	Osteochondroma	Granular periosteal new bone	None	.....	Dead 2 mo. later
37834	W	M	..	Skull, occipital	..	Tumor	Chondroma	.....	Excision	Chondromyxosarcoma	Discharged well
37218	..	M	35	Upper end of humerus	..	Trauma; tumor	.....	Periosteal bone formation	Partial resection	Chondromyxosarcoma	Recurrence; dead 4 yr. after operation
37114	W	F	30	Ribs, right	1	Tumor; pain	Chondroma	.....	Resection	Chondromyxosarcoma	Discharged well
37022	W	F	40	Humerus, upper right	4	Trauma; tumor; pain	Osteochondroma	Translucent periosteal shadow	Resection	Chondromyxosarcoma	Well 10 mo. later
35944	W	M	42	Femur, trochanter	20	Tumor; pain	Osteochondroma	Bone destruction; translucent periosteal shadow	Curettement	Chondromyxosarcoma	Recurrence
35414	W	M	19	Femur, lower	9	Pain; swelling	Osteochondroma	Translucent periosteal shadow with bone destruction	Amputation advised	.....	Well 6 yr. later
34618	W	M	49	Femur, lower, left	2	Pain; pathologic fracture	Chondroma	Translucent periosteal shadow; rarefied bone beneath	Curettement; irradiation	Chondromyxosarcoma	Well 6 yr.
34560	W	M	20	Femur, lower shaft	8	Pain; swelling; tumor	.....	Exostosis and shadow of soft part	Excision; amputation; irradiation	Chondromyxosarcoma	.....
34522	W	F	41	Femur, lower, left	28	Trauma; stiffness; pain	Chondroma	Translucent periosteal shadow; bone destruction beneath	Exploration; amputation	Chondromyxosarcoma	Metastases to frontal bone 4 yr. later
34360	W	F	30	Fibula, lower	1	Tumor	Chondroma	Cystic area of bone destruction	Curettement	Chondromyxosarcoma	Lost
34350	W	M	49	Ilium, right	3	Pain; stiffness	Chondroma	New bone; bone destruction	Excision; radium	Chondromyxosarcoma	Dead 3 yr. later
34166	W	M	51	Pelvis, acetabulum	1	Trauma; pain; tumor	Osteochondroma	Rarefaction; expansion of acetabular margin	No operation	Chondromyxosarcoma	Dead 4½ yr. later; autopsy
33423	W	M	49	Femur, greater trochanter, right	2	Trauma; pain	Chondroma	Translucent periosteal shadow; bone destruction beneath	Curettement (13 times); amputation	Chondromyxosarcoma	Dead 4 yr. later
33052	W	M	25	Tibia, upper shaft	1½	Trauma; pain; pathologic fracture	Chondroma	Translucent shadow of soft part	Exploration; resection; irradiation	Chondromyxosarcoma	Well 7 yr. later
33008	W	F	75	Humerus, upper right	4	Pain; tumor	Chondroma	Translucent periosteal shadow; bone destruction beneath	No operation	Chondromyxosarcoma	Dead 2 yr. later; autopsy
32668	W	M	69	Tibia, upper, left	1	Pain; tumor	Chondroma	Translucent periosteal shadow at tuberosity; diffuse bone destruction of upper shaft	Many curettings; amputation	Chondromyxosarcoma	Well 3 yr.
32485	W	F	90	Ischium, right	3	Tumor; pathologic fracture	Osteochondroma	Granular periosteal new bone	Irradiation	.....	Dead 5 yr. later
32317	W	M	25	Femur, mid-right	1½	Trauma; swelling; pain; tumor	.....	Large calcifying periosteal tumor (exostosis)	Exploration; amputation	Chondromyxosarcoma	Suicide, 1929

TABLE 6.—*Secondary Chondromyxosarcoma—Continued*

Pathologic No.	Race	Sex	Age	Location	Duration, Yrs.	Symptoms	Primary Condition	Roentgenographic Appearance	Treatment	Microscopic Changes	Result of Treatment
30344	W	F	39	Pubis, right	3	Pain; tumor	Osteochondroma	Bone destruction; translucent periosteal shadow	Curettement	Chondromyxosarcoma	Recurrence
30249	W	M	30	Femur, lower	3	Tumor	.....	Metaphyseal widening; periosteal tumor	Exploration	Chondromyxosarcoma	Dead 1 yr. 3 mo. later
30246	W	M	30	Femur, lower	3	Tumor	Osteochondroma (?)	.....	Exploration	Chondromyxosarcoma	Dead 11 mo. later
30186	W	M	40	Femur, lower	..	.....	.....	Rarefaction and cortical expansion of shaft	Amputation	.....	Well 5 yr., lost
29819	W	M	18	Astragulus	4	Pain; tumor	Chondroma	Bone destruction; radiating new bone	Exploration; amputation	Chondromyxosarcoma	Well 5 yr. after amputation
29616	W	M	64	Tibia; fibula; pelvis	½	Trauma; pain	Ossifying periostitis; Paget's disease (?)	Ossifying periostitis; translucent mass in popliteal space	Irradiation; amputation	.....	Dead 7 mo. later
29613	W	F	54	Femur, lower	⅙	Pain; tumor	Osteochondroma	Translucent periosteal shadow over exostosis	Excision (?)	.....	Lost
29559	W	F	53	Humerus, upper	1	Tumor; pain	Osteochondroma	Granular periosteal new bone	Excision; irradiation	Chondromyxosarcoma	Dead 1 mo. later
29467	W	M	29	Humerus, midshaft	..	Tumor and tenderness	Osteochondroma	Translucent periosteal shadow; bone destruction	Resection; roentgen therapy	.....	Well 7 yr. 5 mo.
29382	W	M	42	Ilium, acetabulum	⅙	Trauma; pain	Osteochondroma	Periosteal roughening; bone destruction beneath	Curettement; radium	Chondromyxosarcoma	Dead 9 mo. later
28639	W	F	55	Tibia, upper	¼	Pain; tumor	Chondroma	Translucent periosteal shadow	Amputation	Chondromyxosarcoma	Dead 2 yr. later
28538	W	M	45	Humerus, upper	20	Pain	.....	Tremendous bone destruction; multiple periostitis	.....	Chondromyxosarcoma	Dead; metastasis to bone and lungs
28413	C	F	17	Ninth rib	4	Pain; tumor	Chondroma	.....	Resection (twice)	Chondromyxosarcoma	Well 9 yr. after second operation
28398	W	F	8	Tibia, upper	30	.....	Osteochondroma	Translucent periosteal shadow; bone destruction beneath	Curettement; radium	Chondromyxosarcoma	Well 11 yr.
28246	W	F	41	Vertebra, fourth lumbar	41	Congenital multiple tumors	Multiple chondromas, hereditary	Translucent periosteal shadow; bone destruction; multiple exostoses	Exploration	.....	Dead 2 yr. later
27791	W	M	34	Scapula; spine	7	Trauma; tumor	Chondroma	Rarefied expanded area; bone destruction beneath	Curettement	Chondromyxosarcoma	Lost
27286	W	M	44	Femur, shaft	1/12	Trauma; tumor	.....	.....	Amputation	Chondromyxosarcoma	Well 20 yr. later
27222	W	F	33	Rib at sternum	1	Tumor	Chondroma	.....	Curettement (3 times); radium	Chondromyxosarcoma	Recurrence, lost
26721	W	M	43	Humerus, upper	3	Pain; tumor	Chondroma	Translucent periosteal shadow; bone destruction beneath	Irradiation; resection; amputation	Chondromyxosarcoma	Dead 20 mo. later
25505	W	F	70	Femur, lower	⅙	Pain; tumor	Osteochondroma	Granular periosteal new bone	Amputation	Chondromyxosarcoma	Dead 1 yr. later
23284	W	F	42	Femur, lower	24	Tumor	Osteochondroma; chondrodysplasia	Bone expansion; granular periosteal new bone	.....	.....	Dead 1 yr. later

22929	W	M	40	Astragalus	30	Trauma; tumor; pain	Osteochondroma	Translucent periosteal shadow with new bone	Resection; amputation	Chondromyxosarcoma	Dead 3 yr. later; metastasis to other bones
19545	W	M	43	Os calcis	1	Pain; tumor	Osteochondroma	Translucent periosteal shadow	Curettement; amputation	Chondromyxosarcoma	Recurrence; living 3 yr.
19133	C	M	37	Humerus, upper	2	Pain; tumor	Chondroma	Bone expansion; translucent periosteal shadow	Amputation (2 times)	Chondromyxosarcoma	Dead 10 mo. later
18760	W	M	34	Pubis	1	Tumor	Osteochondroma	Granular periosteal new bone	Resection	Chondromyxosarcoma	Died at operation
15977	W	F	60	Tibia, shaft	3	Tumor; pain	Paget's disease	Osteitis deformans; translucent periosteal shadow; bone destruction	Amputation	Chondromyxosarcoma	Dead 7 mo. later
15395	W	M	49	Sternum, upper	3	Tumor	.....	.....	Partial excision	Chondromyxosarcoma	Well 9 yr. later
15327	W	M	62	Humerus, upper	3	Trauma; pain; tumor; previous abscess	Chondroma	Translucent periosteal shadow; new bone; bone destruction	Amputation	Chondromyxosarcoma	Lost
13511	W	M	24	Jaw, lower, left	2	Tumor	Osteochondroma	Periosteal new bone; bone destruction	Excision (2 times) resection; radium	Chondromyxosarcoma	Recurrence; living 7 yr.
12943	W	M	48	Femur, lower	27	Pain; tumor; pathologic fracture	Osteochondroma	.....	Curettement (2 times); amputation	Chondromyxosarcoma	Dead 3 yr. later
12221	C	M	52	Humerus, lower	14	Pain; tumor	Osteochondroma	.....	Excision	Chondromyxosarcoma	Lost
10150	W	F	35	Femur, lower, left	6	Tumor	Osteochondroma	Granular periosteal new bone; rounded exostosis	Excision	Chondromyxosarcoma	Dead 4 yr. later
10000½	W	M	52	Pelvis	1 & ⅛	Tumor	.....	.....	Exploration	Chondromyxosarcoma	Dead 1 yr. later
9339	W	M	42	Ribs	14	Multiple tumors	Chondromas	.....	Excision	Chondromyxosarcoma	Dead 10 mo. later
8475	C	M	60	Humerus, upper	1	Pain; tumor	Chondroma	.....	Curettement	Chondromyxosarcoma	Dead 4 yr. later
8111	W	M	56	Os calcis, right	25	Pain	.....	.....	Excision; amputation	Chondromyxosarcoma	Recurrence; dead (?)
6773	W	F	60	Humerus, upper	10	Trauma; pain; tumor	Osteochondroma	Exostosis undergoing destruction	Excision (4 times); amputation	Chondromyxosarcoma	Dead 3 yr. after last operation
1972	W	M	51	Femur, lower	3	Stiffness; tumor	Chondroma	Translucent periosteal shadow; bone destruction	Amputation	Chondromyxosarcoma	Dead 3 mo. later
908	W	M	70	Humerus	1 & ⅛	Trauma; pathologic fracture	.....	Periosteal shadow	Amputation	Chondromyxosarcoma	Dead 13 yr. later from other causes
745	W	M	67	Jaw, lower	3	Pain; tumor; extraction of teeth	Osteochondroma	Bone absorption; pathologic fracture	Excision	Chondromyxosarcoma	Well 3 yr., lost
532	W	M	50	Ribs	..	Four repeated fractures of ribs	.....	.....	Excision	Chondromyxosarcoma	Local recurrence; dead 5 wk. after discharge

When this sarcoma develops secondarily in a benign cartilaginous growth, the history of the earliest phases of the disease can usually be elicited by careful questioning. The typical story given by such patients may begin with an injury many years before, the effects of which have subsided without apparent trace, or which remain in the form of a persisting lump of stationary size. There may be a history of rheumatic pains for many years or the consciousness that the affected limb has

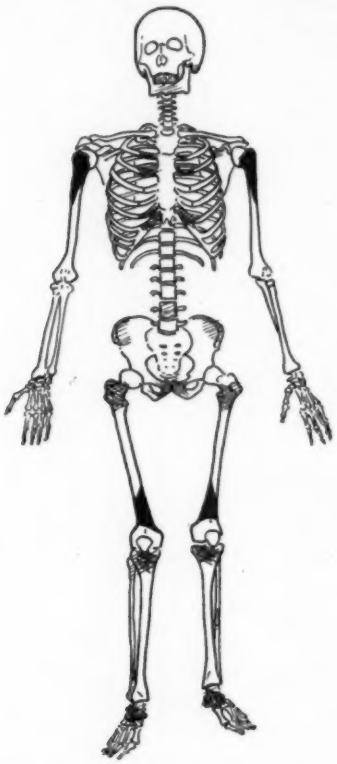

Fig. 56.—Incidence of secondary chondromyxosarcoma according to skeletal location. The solid black areas indicate the most frequent sites; the checked areas, the common sites; the diagonal lines, the occasional or rare sites.

always been crooked or shorter than the corresponding normal member. After an interval of years, and without obvious provocation, pain, swelling or pressure phenomena will cause an exacerbation of the previous trouble and lead the patient to consult his physician. In one instance, a farmer had been kicked in the pubic region by a horse twenty-five years before, and a small stationary tumor had developed. In the two months preceding examination, a rapidly growing pelvic mass (arising

from the pubic bone near the symphysis) had caused pain and edema in the left leg because of blockage of the venous return. A similar case of sarcoma in a woman 50 years of age occurred twenty years after rheumatic pains in the upper part of the arm near the deltoid muscle at the site of an old exostosis.

The actual onset of malignancy in such neoplasms is difficult to establish. In some instances, the first lesion is obviously congenital. Judging from the primary form of this sarcoma and the subsequent rapid clinical course, the malignant change in these secondary tumors does not precede the onset of the acute symptoms by many months. However, the history of the case is often sufficiently vague so that the clinician must be on his guard against making a diagnosis of a benign osteochondroma on the mere circumstances of the long duration of the

TABLE 7.—*Clinical Features of Primary and Secondary Chondrosarcoma*

	Primary	Secondary
Origin	Junction of tendon to bone	Previous benign skeletal tumors
Sex	Males, 2:1	Males, 2:1
Race	Blacks, 15%	Blacks, 6%
Most frequent ages	14 to 21 years	30 to 50 years
Favorite sites	About knee; upper end of humerus	Shoulder and pelvic girdle; knee and heel
Duration of symptoms	3 to 5 months	2 to 25 years
Usual symptoms	Pain; tumor; tenderness	Pain; tumor; tenderness
Trauma	22%	22%
Pathologic fracture	None	6%
Constitutional manifestations	Occasional fever; leukocytosis; enlargement of regional lymph nodes; secondary anemia	Systemic reactions rare; secondary anemia

symptoms given. The degree of pain and the rapidity of the tumor growth are more trustworthy guides from the standpoint of diagnosis, but here again it must be borne in mind that benign exostoses which have been subjected to insufficient operation may, in rare instances, show similar features on recurrence, although no malignant change has taken place. In such instances, the x-ray picture and the biopsy constitute the most conclusive evidence. Nevertheless, it is a good clinical rule always to suspect a secondary chondromyxosarcoma when a history of indefinite rheumatic pains for a period of from five to ten years is obtained from an adult with a lesion in the region of a condyle or tuberosity of a long bone followed recently (in the space of a few weeks) by a change in the character and intensity of the symptoms.

This is well illustrated by a recent case of a physician, 31 years of age, who had a lesion in the internal malleolus of the left tibia (fig. 57). From a roentgenographic standpoint, this tumor was misdiagnosed a benign giant cell tumor. The location in an epiphysis, the central area

of destruction and the age of the patient were consistent with such a diagnosis. However, the patient gave a history of injury and continued weakness with occasional rheumatic pains in the left ankle dating back nineteen years. The acute symptoms of stiffness and soreness had been present only six weeks. This history suggested a secondary chondromyxomatous lesion, which was verified at operation.

Trauma incident to the malignant change occasionally occurs in this group of tumors, but often the injury relates to the original benign

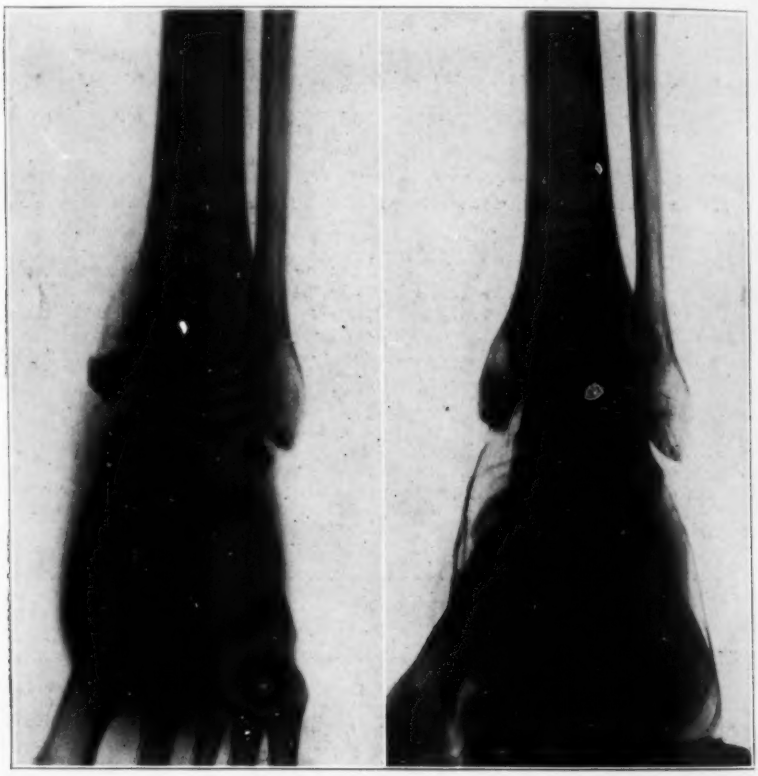

Fig. 57 (P. N. 43022).—Roentgenogram of a small chondromyxosarcoma embedded within the malleolus of the tibia. The patient gave a history of injury and continued weakness in the left ankle at this point dating back nineteen years. The acute symptoms of stiffness and soreness had been present six weeks. The lesion was excised and cauterization with 50 per cent zinc chloride was used. The patient has continued well for seven months.

growth and is to be associated with the incidence of trauma found in exostoses and kindred lesions (from 30 to 40 per cent). Pathologic fracture occurs in 6 per cent of secondary chondrosarcomas, and in these cases the line of fracture often extends through the protruding tumor mass rather than through the body of the bone (fig. 58).

Fig. 58 (P. N. 32317).—Secondary chondromyxosarcoma arising at the site of an old exostosis in a white man, aged 25. The malignant change occurred eighteen months previously, as far as can be determined, following a severe blow to the right thigh by an automobile crank. The tumor was explored, and the sections pronounced chondrosarcoma. Amputation was advised, but refused. The patient carried the tumor for four years longer at which time there was a pathologic fracture, and the tumor had reached such size that the patient consented to amputation, the specimen weighing 72 pounds (32.7 Kg.). The patient remained well two years after operation, despite a transient hemiplegia which occurred postoperatively. Six years after the first examination, however, his health began to fail, he became despondent and committed suicide by multiple stab wounds to the abdomen. Autopsy was not obtained. The roentgenogram shows the original base of the exostosis and the splintering of bone and spotty calcification typical of secondary chondromyxosarcoma.

ROENTGENOGRAPHIC FEATURES*

The most easily recognized secondary chondrosarcoma is that in which distinct evidence of the nature of the primary lesion persists in the x-ray film and in which the superimposed malignant change is visible as a fuzzy infiltrating periosteal shadow. When a previous

Fig. 59 (P. N. 23284).—Roentgenogram of a secondary chondromyxosarcoma in a white woman, aged 44, who had had pain and swelling of increased severity in this region for two years, and who died one year after the picture was taken. The patient refused any form of treatment. The metaphyseal widening in this femur is indicative of a preexisting osteochondroma in this region.

osteochondroma is implicated, the evidence of this original lesion is usually visible in the form of a widened metaphyseal region in the

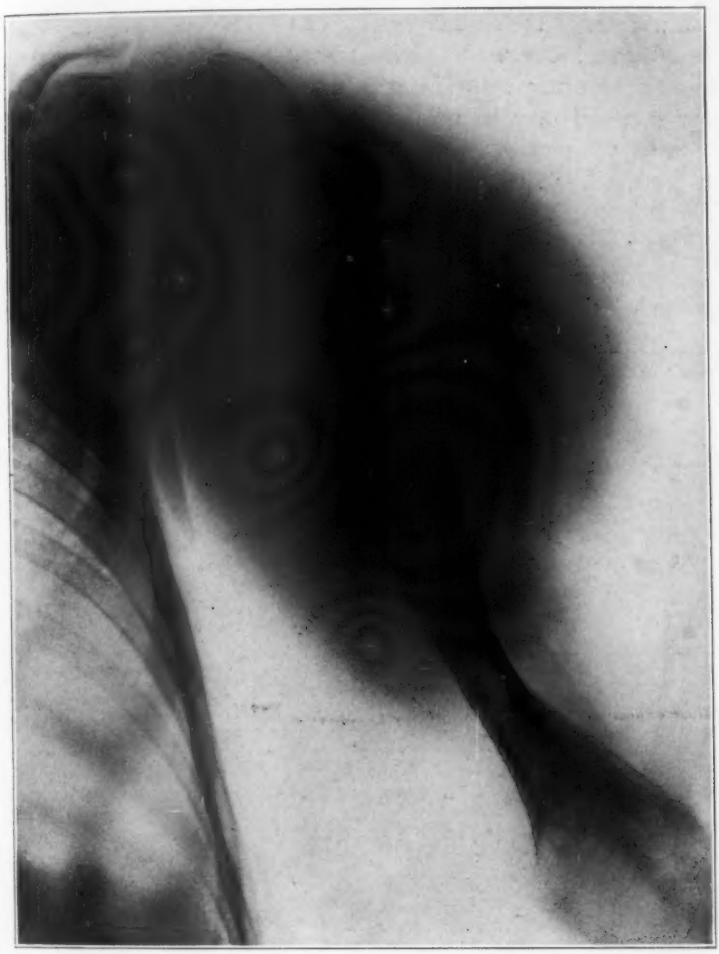

Fig. 60 (P. N. 42888).—Roentgenogram showing beginning malignant change in the upper end of the humerus of a patient who had multiple chondromas of the left hand and a benign chondromatous lesion of the upper end of the humerus. The invasion of the marrow cavity and the pathologic fracture indicate a secondary chondrosarcoma. The patient, who was 50 years old, said that his left arm had always been more crooked and shorter than the right and that the nodules on the left thumb and forefinger shown in the roentgenogram had been present for over forty years. None of these tumors bothered him until two years previously following a fall on the ice. Since that time the upper part of the left arm had been painful, and the swelling there had increased rapidly. A resection of the upper end of the humerus was performed following which the patient died eighteen hours later of postoperative shock.

affected or adjacent bones, and the persistence of the more thoroughly ossified portion of the base or pedicle of the exostosis (figs. 54 and 59).

In advanced cases, the entire tumor site becomes the seat of an infiltrating granular mass in which scattered elements of splintered osseous material may be seen. Destruction of the cortical bone with invasion of the medullary cavity follows, and pathologic fracture may occur (figs. 60, 61, 62 and 63).

The most frequent sources of confusion in the diagnosis of secondary chondromyxosarcoma are benign osteochondromas, myositis ossificans and the sclerosing form of osteogenic sarcoma. The differentiation of this form of chondrosarcoma from a benign exostosis when both are

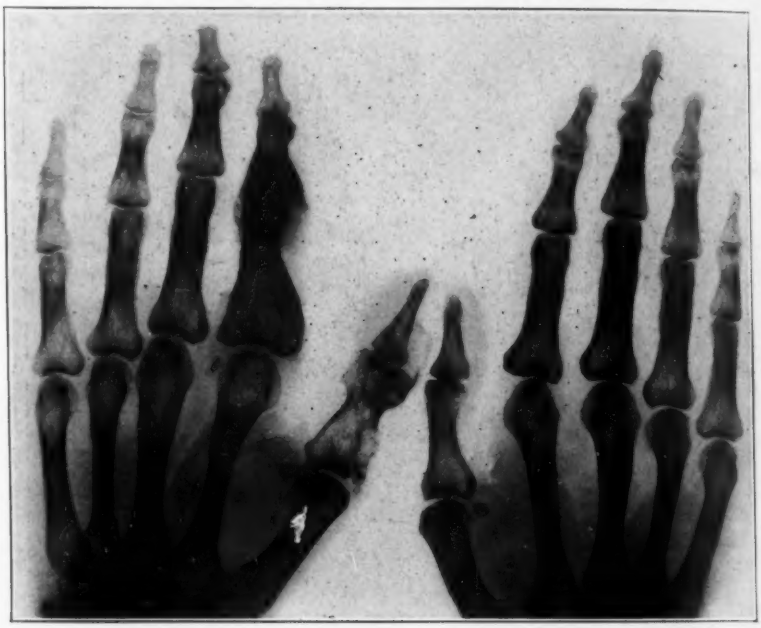

Fig. 61 (P. N. 42888).—Roentgenogram of the hands of the patient shown in figure 61. Note the chondromatous lesions in the left thumb and forefinger.

actually present in the same film is sometimes extremely difficult. The most helpful point is the gradual blotting out of the lines of configuration of the benign lesion from above inward by the malignant change (fig. 54). When the destructive process affecting the bone reaches the medullary cavity, and if pathologic fracture occurs, the diagnosis of malignancy becomes increasingly certain (fig. 60). In myositis ossificans traumatica in which the lesion has been of relatively short duration and has reached a stationary size, the differential diagnosis is not difficult because of the wedge-shaped configuration of the growth and its dense and laminated structure (Lewis [16]). But when

the myositis ossificans becomes progressive and the lesion becomes increasingly dense, shaggy and large, it is difficult to tell whether the growth is still benign or whether secondary chondrosarcoma is present (fig. 64). In such cases the lesion is usually malignant, and the diagnosis should be confirmed by biopsy. Sclerosing osteogenic sarcoma

Fig. 62 (P. N. 42888).—Gross specimen of the resected humerus shown in figure 60. The cartilaginous tumor mass has invaded the shaft of the humerus and produced pathologic fracture visible at the site of the cystic area in the gross specimen, but shown only poorly in the roentgenogram.

is to be distinguished from this secondary form of chondrosarcoma by the greater density of the periosteal shadow and by the fact that it produces sclerosis of the marrow cavity rather than advanced destruction of cancellous bone.

PATHOLOGY AND HISTOGENESIS

As will be seen from the histogenesis of this group of secondary chondrosarcomas, there is no difficulty in tracing a relationship between

Fig. 63 (P. N. 42888).—Microscopic preparation from the tumor mass shown in figure 63. Note the cellular character of the fibrous tissue separating the chondral lobules. This was a frozen section prepared at operation.

the benign osteochondromas and chondromyxomas and this form of sarcoma of the bone. The real difficulty arises in attempting to differentiate these malignant lesions pathologically from the benign cartilagi-

nous tumors from which they arise and to recognize them as secondary forms of chondrosarcoma as distinguished from the primary form.

In many cases, at the operation or in the gross specimen, the evidence of the original benign growth is plainly visible and will have been inferred from the roentgenogram. This is true in cases in which a benign exostosis, hereditary chondrodysplasia, Paget's osteitis deformans or multiple enchondroma are unquestionably present and the malignancy can be seen as a superimposed change with the more recent and rapid growth surrounding the old and more mature process (fig. 65). From an

Fig. 64 (P. N. 27299).—*A* is a roentgenogram of a typical benign case of myositis ossificans; *B* (P. N. 27702) shows a progressive and invasive case of myositis ossificans in which malignant change is to be suspected.

analysis of the gross specimen and microscopic sections, it can be concluded at once that the previous benign cartilaginous growth is only partly responsible for the more recent and more rapidly proliferating chondrosarcoma. By this is meant that the cartilaginous structure or osteochondral mass built up by the preceding benign neoplastic growth does not undergo transformation into sarcoma as a whole, but instead acts as a fossil remains which is gradually destroyed by the new malignant growth arising from the more primitive connective tissue elements that always persist at the periphery of these tumors.

Histologically, this is evident in an emphatic way. At the site where the sarcoma is arising, there is always a reduplication and proliferation of the connective tissue elements, which are present only in insignificant proportions in the benign cartilaginous group and always interspersed with chondral elements in the primary chondrosarcoma. This proliferation of connective tissue in the secondary chondrosarcoma soon takes on a myxomatous character, and it is because of the conspicuous amount of this myxomatous proliferation present at the margin of these secondary sarcomas that Bloodgood originally called attention to them under the term "pure myxoma of bone" (fig. 66).

Fig. 65 (P. N. 39952).—Gross specimen showing a secondary chondromyxosarcoma arising from the periphery of a benign pedicle exostosis in a colored boy, aged 18. Symptoms referable to the original exostosis had been present for over three years. The patient is living twelve months after amputation of the limb. Note that the fibrocartilaginous sarcoma mass not only extends around the dark pedicle of the exostosis but that it is also present in the bulb or cartilaginous cap of the previously benign growth.

Aside from the relatively large amounts of this myxomatous tissue seen under the microscope, and the evidence of preexisting benign growths often found in the gross specimens, secondary chondrosarcoma differs pathologically in no essential way from the primary chondrosarcomas. From the standpoint of microscopic diagnosis, it is at times

difficult to distinguish both the primary and secondary chondrosarcomas from the closely related benign osteochondromas and chondromyxoma. In general, it is helpful to call attention to the more densely cellular and abundant character of the embryonic connective tissue strands, the interspersion of malignant round cells near these connective tissue strands

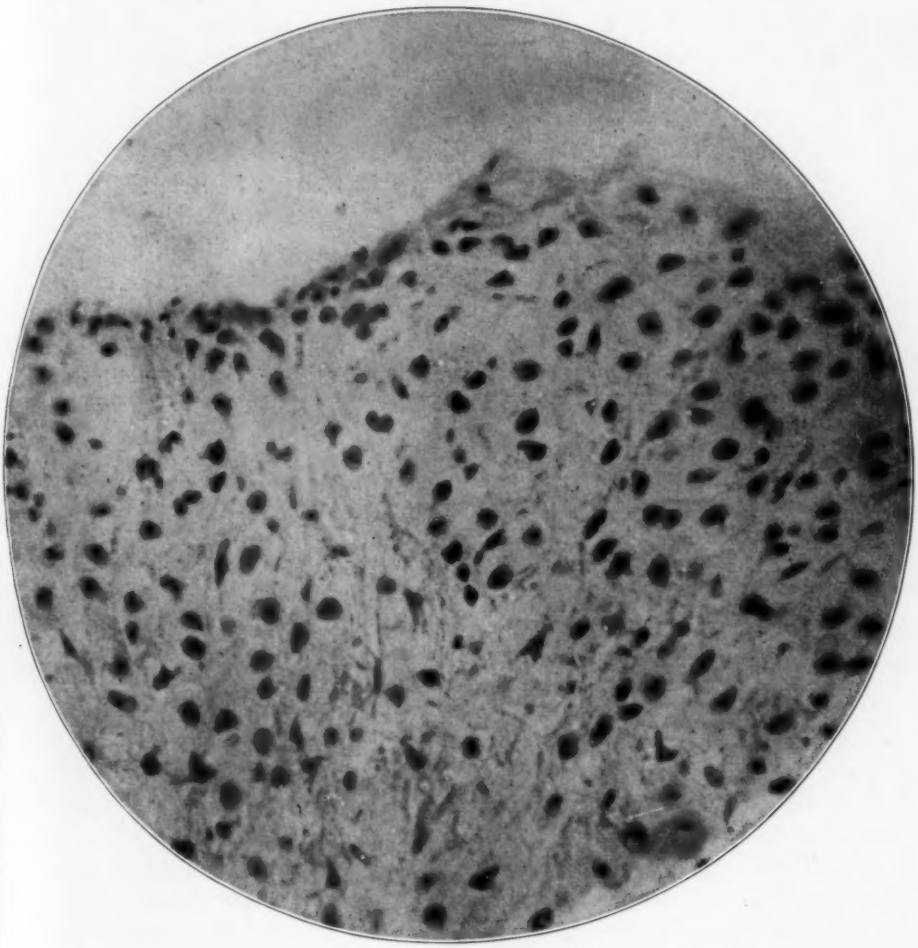

Fig. 66 (P. N. 6773).—Microscopic structure of the lesion shown in figure 54. This portion of the tumor is composed entirely of embryonic precartilaginous connective tissue and fetal cartilage cells, embedded in a hyaline matrix. This is a so-called pure myxoma of bone of Bloodgood.

where they border on myxomatous tissue and the appearance of large multinucleated malignant cartilage cells with mitotic figures amid the chondral lobules, which will be found in the sections of both primary

and secondary chondrosarcoma and absent in benign cartilaginous lesions.

PROGNOSIS AND TREATMENT

When a malignant change has occurred in secondary chondrosarcoma, the average duration of life does not exceed more than two or three years. In a small group of these cases, it is true, the duration may be from four to six years after many recurrences; there are six such cases in this series. In all probability the first recurrence in some of these cases was a benign growth, the malignant change following the recurrence. These secondary malignant tumors grow more slowly than the primary chondrosarcoma and are probably influenced in this matter by the advanced age of the person. If such a tumor is explored and the microscopic section only is submitted for pathologic analysis and prognosis, it is practically impossible to render an accurate opinion because of the gradual gradation from the benign chondromas, on the one hand, and the close resemblance to primary chondrosarcoma, on the other. If

TABLE 8.—*Results of Treatment in Cases of Secondary Chondrosarcoma*

Total number of cases	80
Lost	7
Total number of cases followed	73
Patients followed less than five years and reported well	12
Patients reported dead since 1925	11
Number of cases followed less than five years	23
Total number of cases followed for more than five years	50
Number of patients living over five years	12
Number of patients dead previous to 1925	38
Percentage of five year cures	24%

an x-ray film is available, however, the chances of a cure can be largely estimated by the amount of bone destruction and the extent of the invasion of the marrow cavity by the tumor. The greater the degree of medullary involvement, the worse is the prognosis.

The percentage of actual cures in this form of tumor is 24 per cent (table 8). Of the twelve patients living and well more than five years after treatment, eight were treated by radical resection or amputation. In the other cases, curetting followed by cauterization with the soldering iron and subsequent deep roentgen therapy or radium treatment accomplished a cure. In one of the cases in which a radical resection of the jaw was done after several recurrences following excision, radium was used following the resection.

The remarkable feature in these cases of cure is the effectiveness of radium and the number of recurrences due to ineffective treatment before ultimate recovery was achieved. In one case, which must be looked on as a cure of five years' duration, amputation was performed

four years after the original exploration. In two other cases there were numerous recurrences prior to the amputation or radical resection.

All the patients who were cured except two were over 25 years of age; in two the tumor was at the upper end of the humerus, and in two it extended above the midshaft of the femur. Cures in the upper portion of the humerus or femur speak for low grade malignancy in this type of tumor, since they are extremely rare in this location when the growth is primarily malignant. The actual rôle of the incomplete operation cannot be estimated in any of these cases, since it is possible that the original unsuccessful operations were performed on a benign tumor and a malignant change followed at a later date, closely preceding the final operative procedure. Unfortunately, exact microscopic studies on the tissue from each operation are not at hand to settle this point. However, in view of the many cases that have ultimately proved fatal after recurrences following incomplete operation, it is only fair to assume that radical operation is usually necessary at the outset of the malignant course to effect a cure.

In deciding on the operative procedure, it is well to bear in mind that radium is effective in this form of sarcoma, when complete eradication of the tumor cannot be accomplished by radical resection or amputation. If the tumor is cartilaginous and its benign or malignant nature is in doubt, it is best to excise with the cautery and follow with radium therapy.

CONCLUSIONS

The gradations in a single type of tissue differentiation met with in the osteochondromas (in which bone predominates), in the benign chondroma (in which cartilage predominates) and in the primary and secondary forms of chondromyxosarcoma (in which myxoma and fetal cartilage predominate) seem to imply a close relationship between the formation of tumors and the factors concerned in the growth and differentiation of tissue (table 9).

Apparently all of these various tumors have their origin in a single mother substance, an early precartilaginous connective tissue, and their varying degrees of malignancy are an expression of the rate and extent of differentiation in this tissue. When the rate of differentiation is slow and the extent of cartilage and bone formation is large, a benign exostosis results. When the rate of differentiation is rapid and the amount of adult cartilage and ossification is small, the neoplasms take the form of a chondromyxosarcoma. When an intermediate condition prevails, a benign chondroma, showing a definite tendency to malignant change in many instances, is produced.

In all of these tumors, however, the character of the histogenic cycle is the same, implying that the tissue of origin and not the etiologic agent is the determining factor in this regard. Whether or not the rate and extent of differentiation that governs the degree of malignancy

is predetermined in the tissue at the time of the tumor's origin or whether it is dependent on the etiologic factor precipitating the growth, is difficult to decide. Apparently, however, the etiologic factor is a secondary and variable influence. This is indicated by the fact that the benign exostoses may be accurately duplicated by gonorrheal spurs and arthritic osteophytes of known infectious origin, while similar benign growths such as those in multiple exostoses of the chondrodysplasia type show a definite hereditary tendency. That such widely divergent influences should find expression in a single form of neoplastic process, speaks for the preexistence of a normal growth cycle which may be thus set in motion, and which determines the development and character of the neoplasm.

TABLE 9.—*Leading Clinical Features of Tumors Derived from Precartilaginous Connective Tissue*

Tumor	No. Cases	Age Incidence	Predominant Location	Average Duration of Symptoms	Treatment Recommended	Predominant Microscopic Observations	Average Duration of Life*	Percentage of 5 Year Cures
Exostosis	262	10-25	Lower end of femur; upper and lower end of tibia; upper end of humerus	5 yrs.	None or excision	Adult bone; cartilage	Not affected	95+†
Chondroma	71	20-30	Small bones of hands and feet; ribs; spine	5 yrs.	Curetting with cauterization; radium for recurrence	Adult cartilage	Not affected	95+†
Primary chondromyxosarcoma	79	14-21	Lower end of femur; upper end of tibia; upper end of humerus	6 mos.	Radical excision or amputation and radium postoperatively	Myxoma; fetal cartilage; cartilage and bone	20 months in fatal cases	5
Secondary chondromyxosarcoma	75	35-55	Lower end of femur; upper end of humerus; upper end of femur	6 yrs.	Radical excision or resection and radium implantation	Myxoma; fetal cartilage; cartilage	8-9 years in fatal cases	24

* From onset of symptoms to death.
† There is a definite percentage of malignant change in these cases.

Finally, the fundamental pattern of construction in skeletal tissues (the substitution of connective tissue by cartilage and of cartilage by bone), the order of which is adhered to in evolution, in embryology and in all of the various forms of benign and malignant tumors in the fibrocartilaginous group (fig. 1), indicates an inherent and immutable sequence, which prevails in spite of the avowed lawlessness of tumor growth.

The sequence or order of differentiation that is apparent in this group of tumors of the bone suggests that the formation of the tumor itself is part of the evolutionary process of pattern reproduction, and an expression of the ever present tendency to variation manifested in the derivation of form and pattern throughout the organic world.

A REVIEW OF UROLOGIC SURGERY

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(Continued from page 174)

BLADDER

Tumors.—Caylor [25] stated that so-called papillomas of the urinary bladder should not be considered as benign lesions but as low-grade papillary epitheliomas, for they bear the same relationship to epitheliomas of the bladder as low-grade squamous cell epitheliomas of the lip bear to the more malignant grades of epitheliomas in this organ. The removal of specimens from epitheliomas of the bladder as a diagnostic procedure is important, and the possibility of using diagnoses made from biopsy specimens as a basis for the development of a plan of treatment is emphasized. He also pointed out some salient features of less common malignant lesions of the bladder.

Kretschmer [26] reported 109 unselected cases of carcinoma of the bladder in which surgical diathermy was used. There were 87 men and 22 women in the series, the occurrence of carcinoma of the bladder being about four times as common in men as it is in women. Twenty-five patients (22.9 per cent) died in the hospital; 7 patients (28 per cent) died from pulmonary embolism and 4 (16 per cent) from pneumonia; 8 deaths (32 per cent) were the result of urologic complications: anuria caused 3 deaths, suppurative pyelonephritis 3, and uremia 2. In 70 cases, practically two thirds of the series, the condition was

25. Caylor, H. D.: The Pathology of Malignant Bladder Neoplasms, with Especial Reference to the Grading of Epitheliomas, J. A. M. A. **95**:1736 (Dec. 6) 1930.

26. Kretschmer, H. L.: The Treatment of Carcinoma of the Bladder by Surgical Diathermy: A Report of One Hundred Nine Unselected Cases, J. A. M. A. **95**:1728 (Dec. 6) 1930.

far advanced, and the results from the standpoint of cure were highly unsatisfactory; the mortality rate also was high. In 23 cases in which treatment was instituted relatively early, without much involvement of the wall of the bladder, the results were unusually good.

Smith [27] studied 50 cases of carcinoma of the bladder, in all of which operation was performed within the last ten years. In 11 cases the growth was excised; 15 patients were treated by electrocoagulation and 24 by the implantation of radium. Nine patients in the last group were treated by electrocoagulation of the tumor before the implantation of radium.

Carcinoma of the bladder may be classified in two groups, the deeply infiltrating and the superficial papillary. In the first group, if the growth has not metastasized or extended beyond the wall of the bladder, it may be excised or destroyed with radium with about a 25 per cent chance of cure. If the growth is situated on the trigone or about a ureter, the chances of success are much less than if it is situated in the dome or lateral wall. For these deeply infiltrating growths, diathermy has not seemed particularly suitable; other methods have been preferable. Tumors of the superficial, papillary type are best treated by electrocoagulation. If the bases of the tumors are indurated, they may be irradiated by the implantation of one or two gold or platinum seeds. Although the immediate mortality in this group was only 7 per cent, the later mortality from recurrence was slightly higher than in the group treated by excision or irradiation.

Barringer [28] stated that tumors of the bladder should be classified according to their relative malignancy, so that results can be compared. The papilloma with atypical cells should be regarded as a malignant tumor and so treated. In 127 cases of carcinoma of the bladder in which treatment by radium implantation was given, there were 45 cases of papillary carcinoma, 25 (55.5 per cent) of which were controlled for more than three years. In suprapubic implantation of radium the mortality is between 3 and 4 per cent, whereas in surgical removal the mortality is between 10 and 20 per cent.

Bugbee,[29] in a consideration of tumor of the bladder, stated that the medical profession seems willing to consider all tumors of the bladder as potentially malignant. Even the so-called benign papilloma recurs; it grows by direct extension, invasion or implantation, and its

27. Smith, G. G.: The Treatment of Bladder Carcinoma by Irradiation and Diathermy, J. A. M. A. **95**:1730 (Dec. 6) 1930.

28. Barringer, B. S.: The Radium Treatment of Cancer of the Bladder, J. A. M. A. **95**:1734 (Dec. 6) 1930.

29. Bugbee, H. G.: Discussion of Papers by Kretschmer, Smith, Caylor and Barringer on Tumor of the Bladder, J. A. M. A. **95**:1740 (Dec. 6) 1930.

cells have the characteristics of the cells of low-grade epithelioma. This type of tumor responds readily to fulguration and can be kept under control if thoroughly removed and if the bladder is kept under regular observation. From a practical standpoint, tumors of the bladder can be divided into three groups—papilloma, papillary carcinoma and infiltrating carcinoma—with a definite and accepted line of treatment in the first group only.

[COMPILERS' NOTE.—The present concepts of vesical neoplasia are far from standardized. Although efforts are constantly being made to adapt treatment to the type of lesion based on the grading of tissue removed by biopsy, many still treat the tumors cystoscopically on the basis of their gross appearance. As Caylor and Bugbee pointed out, so-called benign papillomas are being more frequently classified as potential epitheliomas. Treatment by fulguration when they are typical of low-grade or border-line malignancy is accepted almost everywhere. In papillary or infiltrating carcinoma, radium, diathermy and surgery compete for precedence in case reports, the ultimate end-results never being satisfactory. However, in the present situation one should not be too critical of any of these efforts at treatment. Total cystectomy for carcinoma of the bladder is offered as a possible means of cure, since the operation of ureteral transplantation is now being placed on a practical clinical basis.]

Schär [30] stated that the long inhalation of small amounts of naphthylamine is not only detrimental to the organism, but fatal. The harmful effects of such inhalations may be divided into two groups: generalized toxemia and direct irritation.

With general toxemia there are destruction of blood, anemia, a low hemoglobin content, decreased erythrocytes and removal of blood pigments from the spleen, as well as anisocytosis, poikilocytosis and the appearance of Howell-Jolly bodies and normoblasts. As further evidence of toxemia, there is cloudy swelling of the epithelium in the liver and kidneys, with a heavy central disposition of fat in the liver. There may also be leukopenia and lymphocytosis. Some workers in experimental carcinomatosis had already noted lymphocytosis in the early stages; hence lymphocytosis may be a manifestation in the precancerous stage.

With direct irritation, there is a chronic inflammatory process in the lungs involving the alveoli and interstitial tissues. The kidneys disclose chronic interstitial and proliferative nephritis with cloudy swelling of the epithelium.

30. Schär, Werner: Experimentelle Erzeugung von Blasentumoren, Deutsche Ztschr. f. Chir. **226**:81 (July) 1930.

The proliferative reaction with the drug is significant. Certain experimenters have demonstrated malignant changes in the lungs. In some of the experimental animals, a tumor forms in the mucous membrane epithelium of the bladder. This has never been noted in rabbits, probably because they do not live long enough. Schär concluded that processes from papilloma to carcinoma are a direct result of the inhalation of naphthylamine.

Diverticulum.—Briggs [31] stated that although carcinoma and diverticulum of the bladder are common, carcinoma in a diverticulum or on the dome of the bladder is rare. Deming also observed the infrequency of primary carcinoma in a diverticulum of the bladder. Ten cases have been reported, with 9 deaths. All the patients were men, 8 of whom were in the seventh decade.

Briggs reported a case in a man, aged 73, with papillary tumor of the dome of the bladder, and the sessile base of the tumor was in a shallow diverticulum. The neoplasm, the diverticulum and a wide section of the wall of the bladder were removed surgically. Death occurred on the fifty-fifth day after operation, probably from pyelonephritis.

Gill [32] reported a case of carcinoma in a diverticulum of the bladder which was successfully resected. Ten months later the patient was well. He called attention to a rather unusual symptom of diverticula of the bladder in general, which, if it had been considered in this case, might have led to the discovery of the diverticulum before malignancy developed. The patient apparently had been suffering from indigestion for about eight years and had twice sought aid for this trouble. On catheter drainage the feeling of fulness and discomfort in the lower part of the abdomen after eating was entirely relieved. Following operation the patient stated that digestive disturbances disappeared. While the patient was seeking relief from the gastro-intestinal symptoms, signs or symptoms referable to the genito-urinary tract were not present and observers probably gave little thought to the presence of a diverticulum of the bladder as the cause of the abdominal complaint. In making a diagnosis not only the common maladies but the unlikely and rarer lesions that occasionally present themselves should be borne in mind.

Ewell [33] stated that the association of diverticula and a malignant growth of the bladder with secondary involvement of the diverticula

31. Briggs, W. T.: Carcinoma in Diverticulum of the Bladder, J. Urol. **24**:517 (Nov.) 1930.

32. Gill, R. D.: Carcinoma in a Diverticulum of the Bladder; Case Report, J. Urol. **24**:521 (Nov.) 1930.

33. Ewell, G. H.: Primary Carcinoma in a Diverticulum of the Bladder, J. Urol. **24**:649 (Dec.) 1930.

by the malignant process is common. Primary epithelioma of a diverticulum without involvement of the bladder is rare. The diagnosis of a primary malignant process in a diverticulum is not easy unless the tumor can be seen at cystoscopy. A history of hematuria in the presence of a diverticulum is suggestive of malignancy, as well as a demonstrable filling defect in the outline of the diverticulum as shown in the cystogram.

If a malignant process is known to exist in a diverticulum the treatment should be surgical. Hunt expressed the opinion that extirpation of the diverticulum and the growth in the absence of external extension should produce better results so far as cure is concerned than is obtained in primary malignant disease of the bladder. Adequate preoperative treatment with drainage of the bladder is essential to safeguard the patient.

[COMPILERS' NOTE.—Malignant tumors are not uncommon in association with a diverticulum. The infection and inflammation and the occasional irritation from calculi are apparently conducive to the formation of new growths, as the incidence of association of diverticulum and carcinoma is high. Targett described three cases from London museums; in one case the diverticulum contained a large sarcoma, in another a papillomatous tumor, and in the third an epithelioma which grew into the diverticulum from the wall of the bladder. Young reported a case in which a carcinoma was found protruding from a penpoint orifice of the diverticulum. Hofmokl reported a case of a large single diverticulum filled with polypi.]

Lower [34] stated that diverticula in the urinary bladder are usually situated in the lateral wall near the ureters. The diverticulum was in the lateral wall in 62.1 per cent of a series of 151 cases; it was on the posterior wall in 21.2 per cent, rarely in the dome and seldom in the trigone. Diverticula may occur at any age, but they usually occur after the age of 50, as in 81.3 per cent of Lower's 151 cases.

Many cases of calculi associated with diverticula have been reported; the stones may be in the bladder, in the diverticulum or in both, or a dumbbell-shaped stone may lie partly in the bladder and partly in the diverticulum. Malignancy is not a rare complication. In 8 cases of the series a diverticulum was associated with tumor of the bladder, and in 2 of these cases, a papilloma was present in the diverticulum.

Complete excision is the only procedure that leads to permanently satisfactory results. In the reported cases the operative mortality varied from 6 to 8 per cent. In Lower's series, in which excision of

34. Lower, W. E.: Diverticula of the Urinary Bladder, Surg. Gynec. Obst. **52**:324 (Feb. 15) 1931.

the diverticulum was performed, the operative mortality was slightly more than 5 per cent. In a few of the earlier cases, there has been recurrence and a second operation has been performed.

If a radical operation is performed early and before renal impairment has become marked, the prognosis is usually favorable. Whether there will be a recurrence of the diverticulum depends partly on the manner in which the opening into the bladder is closed after the diverticulum is removed, and in part on whether the obstruction to the urinary outflow is eliminated. If the musculature is not well approximated, or if any defect remains, this may be the starting point for a recurrence.

Walters and Mulholland [35] stated that there are three methods of resecting diverticula of the bladder. The first two methods are mainly intravesical operations. In one method the diverticulum is inverted and cut off, and the opening is sutured; the other method is similar, except that a purse-string suture is placed about the neck of the diverticulum before inversion. The third method is by extravesical dissection. Diverticula of the bladder are almost always attached to the adjacent ureter. In order to avoid injury to the ureter it should be remembered that the vesical orifice of the ureter is in close proximity to the opening of the diverticulum into the bladder. All diverticula are associated with definite obstruction of the vesical neck. If the patient is young, the obstruction may be due to cicatricial urethritis; if he is old, it usually is due to hypertrophy of the prostate gland or to a median bar.

Syphilis.—Ajamil [36] reported a case of vegetative syphiloma of the bladder. The capacity of the bladder was small, and when the cystoscope was turned toward the trigone the bladder was found to be hidden completely by a papillomatous mass which extended from the base of the bladder to the neck and to the lower part of the urethra. The remainder of the bladder was only slightly congested around the vertex and lateral walls. Lesions of the trigone were formed by a number of pointed papillae which were set close together; they were slightly transparent in some places, closely resembling intense bullous edema, with a characteristic slight slough on the apex of some of the papillae. The Wassermann reaction of the blood and the Kahn test were negative twice, but examination of the spinal fluid disclosed syphilis.

On the basis of this positive result a final diagnosis of vegetative syphiloma of the bladder, concomitant with prostatic syphilis, was

35. Walters, Waltman; and Mulholland, S. W.: Diverticulum of the Bladder: Report of Six Cases, Proc. Staff Meet., Mayo Clin. **5**:347 (Dec. 3) 1930.

36. Ajamil, L. F.: Vegetative Syphiloma of the Bladder, J. Urol. **25**:53 (Jan.) 1931.

made. Thirty centigrams of neoarsphenamine was injected intravenously. Two days later all vesical symptoms had decreased noticeably; the dysuria and pollakiuria had almost disappeared, the urine was less purulent, and the fever was lower. Three days after the injection cystoscopy revealed that all the papillomatous lesions had disappeared; only slight congestion of the surface of the trigone and vesical neck remained.

Stone.—Mombaerts [37] attempted to ascertain by experimental study why approximately 50 per cent of stones of the bladder are not detected in the roentgenogram, whereas only 1.2 per cent of stones of the kidney (Arcelin) are not detected in the roentgenogram. Regardless of their composition, all stones of the bladder, if examined roentgenologically outside of the body, produce definite shadows. The opacity of a stone is a function of its atomic weight and of its thickness. Density interferes only rarely; a dense stone made of uric acid is less opaque than a porous stone of calcium phosphate. The projection of the shadow of stone on the pubic shadow does not make it less visible. A slight displacement of the shadow during the pose considerably diminishes its visibilty. Liquid in the bladder markedly lessens the shadow of a stone. If stones are put into water and examined by roentgen rays the most opaque ones become indefinite in contour, whereas the less opaque ones disappear. Shadows of any stone will not appear if the quantity of liquid is sufficient, whether it is normal urine, bloody or purulent urine or distilled water. In examination of a full bladder, the most penetrating rays will give better results. Soft parts play the same rôle as water. If the bladder can be filled with air, the opaque stones cast a better shadow. This procedure is not always simple; it is not always reliable and is sometimes harmful. If the bladder is filled with colloidal silver, the slightly opaque stones show better but the others disappear. It is Mombaerts' conclusion that before a roentgenogram is made the bowel should be empty, opium should be used to quiet peristalsis, enemas which may leave water in the rectum should be avoided, the patient should stop breathing, pressure should be applied on the bladder and it should be emptied completely.

[Compilers' Note.—It is well known, yet worthy of emphasis, that in a considerable number of cases the plain roentgenogram fails to reveal the presence of vesical calculi of considerable proportions. Every cystoscopist is occasionally surprised to find an unsuspected stone which the plain roentgenogram failed to reveal. Mombaerts' explanation of

37. Mombaerts, Jean: Pourquoi certains calculs de la vessie sont-ils invisibles à la radiographie? J. d'urol. **28**:113 (Aug.) 1929.

this fact is timely and the preparation of the patient and the technic of exposure that he advised are worthy of trial.]

Neurosis.—Hunner [38] stated that one of his chief contributions toward the solution of the problem of neurosis of the bladder is insistence on a personal study of the urine. In certain cases there may be extreme discomfort of the bladder, with pain reflected to the pelvis and lower part of the abdomen, frequency of urination and nocturnal and diurnal incontinence, although urinalysis may yield negative results and cystoscopy reveal nothing but urethritis or urethritis associated with trigonitis. In more than 200 cases of elusive ulcer, there were 4 or 5 in which, after years of intermittent treatment, symptoms ceased even though the cystoscopic picture was similar to the one present for years. In about the same number of cases healing had apparently been complete. Cystoscopic examination did not reveal a trace of inflammation except the white scars of former ulcerous areas, and the urine was normal.

One of the simplest methods of effective treatment for elusive ulcer is the instillation of a 1:500 solution of silver nitrate twice a week, 30 cc. being left in the bladder. Some patients obtain more relief from the direct application to the ulcerous area of a 10 per cent solution of silver nitrate. In many cases the relief lasts for four or five weeks, when symptoms become worse and require another treatment. Hunner preferred fulguration under complete narcosis when simpler devices fail to give satisfactory relief. In most cases benefit from this treatment lasts from six months to two years.

It is probable that the ulcer recurred in 6 of 25 cases in which operation was performed; time will probably show a large percentage of recurrence. In his series of 137 cases of elusive ulcer, operation was performed in 48. One patient died as a result of inefficient care after operation and 26 patients (42 per cent) were known to have recurrence. He had not performed operations for this condition since gathering these statistics.

In 100 consecutive cases of ureteral stricture, vesical symptoms were present in 71. In 33 of these the symptoms were marked and more or less constant, and in 38 they were mild. Many of the patients had rather severe vesical symptoms during attacks of renal pain owing to partial or complete closure of the stricture. In a series of 100 cases of ureteritis, infiltration of the urethra occurred in 85.

In more than 250 cases of partial or complete incontinence, ureteral stricture was usually found to be the cause. Good results have been obtained in most cases by restoring good drainage of the kidney or

38. Hunner, G. L.: Neurosis of the Bladder, J. Urol. **24**:567 (Dec.) 1930.

by the elimination of distant focal infection. Excellent results followed the treatment of nocturnal incontinence of children by tonsillectomy.

Dermoid Cyst.—Kalo [39] noted the rarity of dermoid cysts of the bladder. The literature reveals that they may occur in almost any organ, but they usually occur in the ovary and adjacent regions. Kalo reported a case in which he expressed the belief that the cyst originated in the right ovary. The patient, a woman, aged 57, had had urinary difficulty for many months. The urine was cloudy and infected. It became clear following irrigation of the bladder. It contained droplets of cholesterol-like substances. Above the right ureteral orifice was an opening from which came cloudy turbid material, as well as hair; this was especially pronounced on suprapubic pressure. A cystogram revealed a shadow about 7 cm. in diameter to the right of the bladder. A tumor was removed at operation; it was 5 by 7 cm. and contained bone and hair. Evidence of malignancy was not found.

Kalo noted only two similar cases in the literature. Delore and Alimartin reported a case of left ovarian origin in a woman, aged 58. Rejschek reported a case in a woman, aged 37. Kalo stated that the invasion through the wall of the bladder might be considered as evidence of malignancy, although microscopic evidence of malignancy was not found.

Appendiceal Fistula.—Chauvin [40] reported a case of cecovesical fistula of simple inflammatory origin. This lesion is much less common than fistulas of tuberculous or neoplastic origin. Inflammatory fistulas often permit complete and satisfactory surgical treatment, that is, suture of the bladder and of the intestine after resection of the fistulous tract. Appendicitis is the most common cause of inflammation; it was the cause in 4 of 23 of Albano's cases of nontraumatic fistula, in 6 of 32 of Pristavesco's cases, in 3 of 57 of Douglas' cases, and in 9 of 292 of Pascal's cases. The abscess of the appendix may unite a mass of intestinal loops and these may be in contact with the bladder; consequently, the communication between the bladder and the intestine may be found far from the ileocecum. The diagnosis of this disease is simple when three characteristic symptoms are present: (1) the transit of fecal matter into the bladder or the presence of urine in the bowel, (2) pneumaturia or (3) a fistulous opening in the bladder discovered at cystoscopic examination.

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39. Kalo, Andreas: In die Blase perforierende Dermoidcyste, Ztschr. f. Urol. **24**:330, 1930.

40. Chauvin, E.: Fistule caeco-vésicale d'origine appendiculaire, Bull. et mém. Soc. nat. d. chir. **56**:559 (April 9) 1930.

[COMPILERS' NOTE.—Fistulas may arise between the bladder and rectum, colon, ileum, cecum or appendix. Trauma during operation or accidental injury may be the cause. Inflammatory rupture from the viscus into the bladder may occur. More often tuberculosis or neoplasia is responsible for the spontaneous development of fistula. Pascal, Craig and Lee Brown, and Bryan have written extensively on the subject. Rectovesical fistula was found in 135 of 195 cases. Separation of the bladder and intestine with suture is usually followed by good results in the absence of tuberculosis and actinomycosis. The prognosis in cases of neoplasia depends on whether the tumor can be resected completely.]

PROSTATE GLAND

Hypertrophy.—Thomson-Walker [41] stated that when McGill first advocated the suprapubic operation for prostatectomy, it was generally accepted that about 30 per cent of all men more than 55 years of age had abnormally large prostatic glands, but that only about 50 per cent of them had significant symptoms. Unless there was frequency of urination due to infection of the bladder or partial or total retention of urine, the enlargement of the gland might be disregarded. Infection and retention demanded surgical aid, which was afforded by the occasional or the habitual passage of the catheter. Patients with enlarged prostate glands were taught to pass a soft catheter and were instructed to pass it once or twice a day. The introduction by Mercier of the coudé or curved gum-elastic catheter was to be a great step in treatment in these cases. The cumbersome mahogany case holding catheters was eliminated, and patients carried one catheter in their walking-sticks or umbrella-sticks.

Treatment with a catheter was not always successful. In certain cases the difficulty of a much distorted prostatic urethra or the inability of the patient to learn to pass the catheter prevented the adoption of this method. In acute retention of urine a metal catheter might be forced through the obstruction, tearing through the gland and forming a new channel. Tapping the bladder with a metal trocar and cannula above the pubes, in the perineum or through the rectum, was the common method of treatment.

McGill noted three cases in which suprapubic operation had been successfully performed for chronic prostatic hypertrophy. The operation consisted of opening the bladder and removing that portion of a hypertrophied prostate gland which prevented the passage of the urine from the bladder into the urethral canal.

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41. Thomson-Walker, John: Enlarged Prostate and Prostatectomy, Lancet **1**:1163 (May 31) 1930.

Gouley, of New York, was the first to formulate a plan for perineal prostatectomy. The intravesical enlargement of the prostate gland is first explored through an external perineal urethrotomy wound. If a median outgrowth or isolated tumors are discovered, the prostatic urethra is dilated and incised laterally and the outgrowths are removed, preferably by an ecraseur. Harrison recommended a similar operation with subsequent prolonged drainage.

White noted that in about 20 per cent of cases following suprapubic prostatectomy the bladder does not regain power. He considered that possibly the analogy between uterine fibromyoma and prostatic overgrowth is a real one. Castration might have the same effect on the latter that oophorectomy has on the former, and cause shrinkage or atrophy that would result practically in the disappearance of the obstruction. He did not have the courage of his convictions and never seriously recommended the operation. Others acted on his hypothesis and the operation of castration as a method of treatment for prostatic obstruction was practiced generally.

The mortality caused by suprapubic prostatectomy in McGill's 24 cases was 16.6 per cent. Belfield, in 1890, placed the mortality from the operation at 13.6 per cent. The mortality after castration, which White had expected would be negligible, was 19.4 per cent.

The renaissance of prostatic surgery occurred during 1900 and 1901. Prostatectomy, both by the perineal and by the suprapubic route, found new advocates, and expanded to become the accepted method of treatment for prostatic obstruction. The handicap of the perineal operation had been the difficulty of reaching the gland by this route. In America, Young had been the chief advocate of the perineal operation, and it is due to his advocacy and fine record of results that perineal prostatectomy retains a place among American surgeons. In 1901, Freyer reported four cases in which he operated for radical cure of the enlarged organ by total extirpation. The method described by Freyer was at once adopted by surgeons all over the world.

As a result of watching these cases and from his own experience, it seemed to Thomson-Walker that hemorrhage, if not the direct cause of death in many cases, is a predisposing factor. Although the removal of the prostatic urethra was usually not attended by the risk of traumatic stricture, there were, unfortunately, numerous exceptions; the traumatic stricture of the urethra that followed prostatectomy was difficult to treat. Thomson-Walker also realized that among other points in technic a clean cavity, without capsular shreds or partly detached masses of prostatic tissue and mucosa, was necessary in order to prevent persistent infection after the operation. Keeping in mind the defects of Freyer's operation, he introduced (1916) a method of open operation,

in the hope of preventing the occurrence of such complications. He has used the method in an increasing number of cases until it has become his routine practice. The operation avoids placing the finger in the rectum, and hemorrhage is controlled by free exposure and ligature. All tags, flaps and nodules that might cause sepsis or postoperative obstruction are removed, and the prostatic vesical orifice is opened to prevent contraction.

Chynoweth [42] stated that in a study of 500 patients with urologic disorders, aged from 28 to 84 years, approximately 70 per cent had some form of prostatic disease. Of these 70 per cent, 60 per cent gave a definite history of venereal disease and almost 10 per cent had infections of the teeth or tonsils or both. Two or more pus cells to the field were found in approximately 60 per cent of the prostatic smears. In 12 per cent of these cases a diagnosis was made of simple congestion of the prostate gland. The ages of the patients ranged from 28 to 45. In 50 per cent of the cases benign prostatic hypertrophy was sufficient to cause urinary retention; in 12 per cent retention was complete. Of the cases of prostatic hypertrophy 53 per cent were extravesical enlargement, palpable by rectal examination; 20 per cent were combined intravesical and extravesical enlargement, determined by cystoscopy and rectal examination; 10 per cent were of the intravesical type, as ascertained by cystoscopy and rectal palpation, and 12 per cent were bar obstructions with or without involvement of the lateral lobe. Prostatic bar enlargement is usually associated with fibrosis at the neck of the bladder. In 5 per cent of the series of 500 cases the condition of the prostate gland was malignant.

The size of the gland as determined by examination of the rectum and prostate gland does not always indicate the degree of obstruction produced and does not give complete information as to the condition of the gland. Certain adenomas grow rapidly and produce obstruction; others grow gradually. In this series 22 per cent of the prostate glands were found to be normal by rectal palpation; in 20 per cent the enlargement was noted by cystoscopic as well as by rectal examination.

As a rule, in the presence of persistent residual urine of 60 cc. or more, the prostatic condition tends to progress, and surgical procedures are indicated in most cases. If surgical treatment is indicated it should be undertaken before renal function is impaired. A comparatively simple operation if not done in time may be dangerous. Interference with renal function means inefficient elimination of waste

42. Chynoweth, W. R.: Prostatic Obstruction Caused by Intra-Extra Vesical Hypertrophy; Review of 500 Cases, J. Urol. **24**:669 (Dec.) 1930.

products and favors toxemia which affects all tissues of the body, inducing the final stage of uremia.

Spinal anesthesia was chosen for 90 per cent of the prostatectomies, thus minimizing postoperative renal depression, gastro-intestinal distress and pulmonary complications. In the other 10 per cent of cases gas anesthesia was used.

Gibson [43] stated that primary closure and healing are applicable to wounds of perineal prostatectomy, and that closure can be made the rule rather than the exception. Gauze packs or distensible rubber bags for hemostatic purposes both offer a number of objections: They stretch open still farther the dilated prostatic cavity, which under ideal conditions should be permitted to collapse and shrink as soon as the gland is removed; they cause the patient discomfort, not only by their presence but by their removal, and they delay healing by leaving, on their withdrawal, a temporary urinary fistula, which requires ordinarily from two to four weeks to close.

Before primary closure can be done safely, all bleeding must be carefully controlled. The wound can then be closed tight without drainage, the urinary stream being taken care of by means of a retention catheter through the urethra. If bleeding cannot be checked satisfactorily by suture, the prostatic fossa must be packed with gauze strips.

In perineal prostatectomy it is generally possible to get an adequate view of the neck of the bladder, and in most cases closure can be made without either packs or bags. In a consecutive series of 20 cases of perineal prostatectomy Gibson made a primary closure successfully in 13. In the other 7 cases he was compelled to resort to packs to check the bleeding completely. Analyzing the two groups of cases with respect to the duration of postoperative convalescence, the average time spent in the hospital by patients for whom packs were used was twenty-two days. In cases of primary closure in which packs were not used the average time in the hospital after operation was sixteen days.

[COMPILERS' NOTE.—Young described a technic of primary closure in perineal prostatectomy. Lower and Harris adapted primary closure to the suprapubic operation with reasonable success. Gibson, independently of Young, developed a similar technic. In spite of the theoretical arguments in favor of primary closure as an ideal procedure, it is slow in gaining popularity. Reconstructive operations that tend to obliterate the prostatic fossa after prostatectomy are difficult of application, and the end-results of even the most enthusiastic advocates of the method are not consistently good. At best, Gibson saves less than

43. Gibson, T. E.: Primary Closure in Prostatectomy, Ann. Surg. **92**:82 (July) 1930.

a week in the hospital in about 60 per cent of his cases, and avoids some transient pain. We consider the operation of primary closure an ideal objective but still in the developmental stage. Much more clinical experience with the procedure will be necessary to give it proper evaluation.]

Carcinoma.—Colston [44] divided carcinoma of the prostate gland into three groups: 1. Cases suitable for radical operation. Since carcinoma of the prostate gland in the earliest stages does not cause symptoms, the cases in this group are few. The growth may be comparatively small and limited to the gland. If a radical operation is to be performed satisfactorily the growth must not have extended beyond the capsule, into the seminal vesicles or to the base of the bladder.

2. Cases of carcinoma without obstruction, in which the growth has extended usually upward into the seminal vesicles and pelvic lymph-nodes, or to the base of the bladder. Metastasis to the bones of the pelvis or lumbar spine may or may not be present. Patients with this type of growth are best treated by a combination of radium and roentgen rays. In many of these cases, death from cachexia and widespread metastasis may occur with little if any increase in the size of the original tumor.

3. Cases with more or less urinary obstruction, with or without metastasis to bone. Conservative perineal prostatectomy or the punch operation are best in these cases. Of 268 cases of carcinoma of the prostate gland seen at the Brady Clinic between 1922 and 1927, the conservative perineal prostatectomy was performed in 107, the punch operation in 25 and the radical operation in 13; radium and roentgen rays were used in 65, and in 56 treatment was not given.

Conservative perineal prostatectomy is carried out under caudal anesthesia, which has resulted in a decrease in the mortality. In the 107 cases there were 8 operative deaths (7.5 per cent), about twice the mortality in the benign cases. It was noted that deaths from pneumonia occurred before caudal anesthesia was used as a routine measure. Of the 99 patients who survived operation, only 34 have been traced; 13 of the 34 died within a year after operation, 8 died within two years and 1 died four years after operation. One patient is living, without symptoms, seven years after operation, another is living six years, another five years, another three years, and 8 patients are living two years, after operation; 4 of these 8 are without symptoms, 1 has partial incontinence and 3 have slight frequency and occasional hematuria.

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44. Colston, J. A. C.: Treatment of Urinary Obstruction Due to Malignant Disease of the Prostate, J. Urol. **24**:656 (Dec.) 1930.

The postoperative course is approximately the same as in benign cases. A catheter is usually left in the urethra and withdrawn about the tenth day. There is a varying degree of incontinence which may persist for several weeks after urethral voiding has been reestablished. Of the 12 patients living more than two years after operation, only 1 has partial incontinence.

The ultimate outcome in malignant disease of the prostate gland is poor. In a certain proportion of cases a lasting functional result can be obtained which will restore the patient to a comparatively normal life, and no other operative procedure will give such satisfactory results as perineal prostatectomy. If left alone, these patients die of urinary obstruction, and if subjected to suprapubic cystostomy, invalidism is the result.

Sarcoma.—Raap [45] stated that in 50 per cent of the reported cases of sarcoma of the prostate gland surgical treatment was given. Kretschmer found 80 cases of sarcoma of the prostate gland previous to 1926. Deming, in 1924, collected 65 cases with an extensive bibliography, and stated that sarcoma was present in about 56.9 per cent. The classification included sarcoma, myxosarcoma, fibrosarcoma and lymphosarcoma. Myxosarcoma constituted 25 per cent of the cases, fibroma constituted about 7 per cent, and there was an occasional myoma, rhabdomyoma, fibroma, papilloma, polyp and dermoid. Angiosarcoma and chondrosarcoma have also been reported.

Albarran found that of 252 primary tumors of the bladder, 211 occurred in males and 41 in females; only 6 of the patients were less than 10 years. One of the youngest patients, a girl aged 11 months, had a sarcoma in the bladder. This case was reported by Concetti.

Raap reported the case of a boy, aged 4 months, with urinary retention for one month. Catheterization revealed a grating obstruction in the posterior urethra. On rectal examination a tumor in the prostatic area was definitely outlined. Suprapubic cystotomy was performed. The patient died several weeks later and necropsy revealed extensive prostatic myxosarcoma, together with bilateral hydronephrosis and hydro-ureter.

[COMPILERS' NOTE.—In Young's opinion the condition is rare, and primary sarcoma of the prostate gland is frequently mistaken for sarcoma arising in the retroprostatic tissues. A satisfactory method of treatment has not been found. Palliation by surgical procedures or roentgenotherapy is preferred at present.]

45. Raap, Gerard: Sarcoma of the Prostatic Area in an Infant Aged Four Months; Case Report, Am. J. Roentgenol. **24**:185, 1930.

PENIS

Carcinoma.—Mauclaire [46] stated that in the diagnosis of carcinoma of the penis syphilis must always be considered. The technic he advocated in 1903 was the complete extirpation en bloc of the tumor, of the principal superficial lymphatic territory and of the inguinocrural glands on both sides. In the benign forms, the inguinocrural glands are often inflammatory. Majaux stated that these glands are neoplastic in from 30 to 40 per cent of the cases. In some malignant forms complete extirpation of the lymphatics is justified. In such cases, as in cases of carcinoma of the breast, operation should include complete extirpation of the infected regions, tumor, principal superficial lymphatics and bilateral nodes. The deep lymphatic vessels of the breast must be left in place. Complete extirpation of inguinocrural glands necessitates a large wound and sometimes troublesome scarring. The wound often suppurates. Packing the wound instead of suturing is advocated. Mauclaire stated that elephantiasis may develop in the upper part of the thigh after removal of the lymphatics.

Ferry [47] reported a case in a man aged 78, who had a carcinoma of the penis following an operation for phimosis and balanitis. The tumor was treated by radium; the cure was rapid and has been maintained for four years. Monod, in discussing this case, stated that carcinoma of the penis is a rare lesion in France, representing only from 2 to 3 per cent of all carcinomas, and affecting only patients who had suffered from phimosis. In India and Indo-China, this lesion is more common, comprising 17.5 per cent of all carcinomas. The significance of phimosis as a cause is also demonstrated by the fact that the disease is almost totally absent among Mahometans. Syphilis is also a cause of carcinoma of the penis. Le Roy des Barres, who has had much experience in the matter, has observed it in 50 per cent of cases. The lesion of syphilis resembles epithelioma of the skin. Its evolution is slow, taking three years as an average, although Ferrari has reported cases of twenty years' duration. Recurrence is common, but localized. Distant metastasis is rare. Enlarged inguinal lymph nodes, often inflammatory, have been found in 70 per cent of cases; in Monod's cases they have always been noncarcinomatous.

Two methods of treatment may be used: operation and roentgenotherapy. The surgical treatment consists in removing the tumor, care being taken to amputate as little of the penis as possible. It is still

46. Mauclaire: À propos du traitement du cancer du pénis, Bull. et mém. Soc. nat. d. chir. **56**:710 (June 7) 1930.

47. Ferry, G.: Les indications thérapeutiques actuelles du cancer de la verge: À propos d'un cas guéri depuis quatre ans et demi, Bull. et mém. Soc. nat. d. chir. **56**:618-627 (May 14) 1930.

undecided whether the inguinal lymph nodes should be removed. Le Roy des Barres does not remove them. Biopsy may be performed and, if necessary, the nodes can be removed later; often this will not be necessary. In the opinion of Ferry, Ferrari and Le Roy des Barres, but contrary to general opinion, roentgenotherapy gives excellent results in carcinoma of the penis. Radium usually leaves a normally functioning organ. From the Institut du Radium the following statistics are noted: The end-results were traced in 16 cases. In 9 cure was complete; in 1 case there was improvement and in 5 cases failure; thus cure was obtained in 60 per cent of cases, lasting from three to eleven years. The surgical statistics from Legueu and Kuttner, in 1908, at the International Congress of Surgery give only 30 per cent of cases without recurrences (traced less than four years).

[COMPILERS' NOTE.—A fair opportunity for cure of carcinoma of the penis is afforded by surgical procedures or the application of radium if the lesion is recognized early. Increasing evidence is available to show the superiority of radium treatment if applied properly, and before the growth has penetrated Buck's fascia or metastasized to the inguinal or possibly to the deep pelvic lymph-nodes. The articles of Mauclaire and Ferry bring out the factors to be considered in the use of surgery and radium. Whether the inguinal glands are to be dissected out is a moot point. Those advocating radical operation will certainly feel that biopsy which shows definite metastasis would be an indication for radical dissection. Advocates of roentgenotherapy believe that this form of treatment is sufficient, that it maintains function of the organ and more cures for three or more years.]

TESTIS, EPIDIDYMIS AND SEMINAL VESICLE

Tuberculosis.—Felsenreich [48] stated that the treatment for tuberculosis of the epididymis is still an important problem. Several methods of treatment are employed: the radical method, castration and semicastration; a conservative operation, partial or complete epididymectomy, curetting or incision; roentgen therapy, and the conservative regimen with sunshine and similar measures.

There were 235 proved cases of tuberculosis of the epididymis. One hundred ninety-seven of the patients were observed after operation and carefully traced. Three methods of treatment were used: operative, such as semicastration, castration, and epididymectomy; roentgenotherapy, including roentgen rays and sunshine; injections of iodine compounds, and baths and compresses.

48. Felsenreich, Fritz: Die Therapie der Nebenhodentuberkulose und ihre Fernresultate, Deutsche Ztschr. f. Chir. **224**:383, 1930.

There were 61 cases in the first group. Three years after operation 45 per cent of the patients were free from recurrence. Most recurrences occurred within the first three years after operation.

There were 50 cases in the second group. The patients were given roentgen treatment. It was found that frequent small doses were most satisfactory, the temperature, general reaction, increased pain and swelling being utilized as indicators of the treatment. In 34 cases, 32 per cent of the patients were free from recurrences; in 26 per cent recurrence developed within three months and in 42 per cent it developed later. In this group 8 patients died, 6 from pulmonary tuberculosis and 2 from miliary tuberculosis. From the results in these cases Felsenreich stated the belief that better results could be obtained with roentgenotherapy in the presence of severe pulmonary involvement than with surgical procedures.

The third group consisted of 38 cases. Most of the treatment consisted of conservative local measures, such as the use of iodine ointments and sunlight. The severest cases were included in this group and the mortality was 40 per cent within the first two years of observation. In the entire series, patients who died or who had recurrence had pulmonary tuberculosis. Felsenreich concluded, with Bier, that surgical tuberculosis affects the entire body, that it is in reality metastasis in most cases. The consideration of surgical tuberculosis must be preceded by the study and care of the entire organism.

Tumors of the Testis.—Champlin [49] stated: "Similar tumors in identical (uniovular) twins have been reported rarely. Similar disease has been observed in twins more frequently. It is reasonable to suppose that fetal rest tumors especially could occur in both of uniovular twins. The identical twins presented here both developed sarcoma of the right testicle—fatal in one on account of delay in treatment and in the other apparently cured by early removal."

Sterility.—Hagner [50] considered sterility of the male mainly from the standpoint of operative correction. In most cases failure of impregnation is due to the female. Statistics show that the male is at fault in about 1 case in 6.

Sixty-seven operations were performed in 55 cases. Twelve patients were operated on a second time because of initial failure; 7 of the 12 were cured by the second operation. The results in 4 of the 55 cases were not reported. The condition of 20 patients was discovered at

49. Champlin, H. W.: Similar Tumors of Testis Occurring in Identical Twins, J. A. M. A. **95**:96 (July 12) 1930.

50. Hagner, F. R.: Sterility in the Male, Surg. Gynec. Obst. **52**:330 (Feb. 15) 1931.

the exploratory operation to be inoperable because of occlusion of the vas or absence of spermatozoa in the epididymis. Of the remaining 31 patients, 19 (61.3 per cent) were cured, including the patients reoperated on; 12 of the 19 patients cured became fathers of from one to six children, and in 1 case impregnation was followed by a miscarriage.

Calcification of the Vasa Deferentia.—Bianchini [51] reported the case of a man, aged 34, who complained only of hematuria; he had no other subjective or objective symptoms. The roentgenogram showed almost complete calcification of the vasa deferentia. The patient was not syphilitic and had been well up to the age of 19, when he had tuberculous epididymitis and a local cold abscess was opened. This and general systemic treatment effected a cure. He had been married for thirteen years, and his wife had had an abortion in the fifth month ten years before examination. Eight years before examination she had a child, who was living and well. Bianchini believed that the tuberculous epididymitis caused the almost total calcification of the vasa deferentia. Obstruction of the vasa deferentia had developed slowly; it had not become complete until recent years.

ANESTHESIA

Bumpus [52] stated that the use of spinal anesthesia became more general as a result of the development of less toxic drugs than cocaine. Delaup, in 1910, reported 1,239 cases; in 585 cases, operation was for genito-urinary conditions. Richards, in 1911, reported 500 cases, in 219 of which operation was required for urologic conditions. Pauchet, in 1913, stated that he had used spinal anesthesia in 300 cases for prostatectomy; that it decreased hemorrhage, gave complete abdominal relaxation and rendered enucleation easy. The same year Morrison reviewed 1,295 operations, many of them performed for urologic conditions, including 43 operations on the kidneys, and noted that the danger incidental to spinal anesthesia was in lowering the blood pressure. Chute, in 1922, reported 328 cases of prostatectomy in which he employed spinal anesthesia without serious complications attributable to the anesthetic. Labat emphasized that the danger of spinal anesthesia is not from the fall in blood pressure, except when it produces cerebral anemia, but is attributable to the increased volume of blood in the viscera, due to splanchnic paralysis and vasomotor collapse. He expressed the belief that this cerebral anemia can be avoided by placing the patient in the Trendelenburg position immediately following the

51. Bianchini, A.: Su di un caso di calcificazione quasi total delle vie deferenziali, Arch. di radiol. **6**:228 (Jan.-Feb.) 1930.

52. Bumpus, H. C., Jr.: History of Regional Anesthesia in Urology, J. A. M. A. **96**:83 (Jan. 10) 1931.

intraspinal injection. Keyes, in 1928, stated that spinal anesthesia is admirably suited to all operations on the bladder. For five years he had used capsules containing 120 mg. of procaine hydrochloride crystals, without fatalities.

The first attempts at prostatectomy under parasacral anesthesia were made in 1907. Farr experienced failure in 10 per cent of cases when the method was used for perineal and rectal operations. He supplemented parasacral anesthesia with local infiltration which, in the case of prostatectomy, had to be extended to the capsule.

Stoeckel, in 1909, published the results of a series of injections into the sacral canal during labor, and called the method sacral anesthesia. Lewis, in 1916, reported 85 cases in which he had used sacral anesthesia, with failure in 15 per cent. Pickins, in 1916, reported 81 perfect results and 17 failures in a series of 100 cases. Labat introduced the combined method of caudal block and transsacral anesthesia.

The early methods of application of cocaine for urethral anesthesia were by injection in solution, and this remains the most common method of administration. Randall, in 1923, reported 5 deaths and 25 cases of alarming toxicity due to the use of cocaine in the urethra. There is a wide divergence of opinion on the use of cocaine for urethral anesthesia. Gardner reported the use of cocaine for eighteen years in approximately 50,000 cases without ill effect, and Walther also did not observe serious reaction. Livermore and Crowell reported 3 deaths. Keyes stated that cocaine should never be used in the urethra. At the Mayo Clinic it has been employed for cystoscopic examinations during the last ten years with satisfactory results. Klotz reported 102 deaths from cocaine; in one instance it was administered by instillation. The important question is the dosage and the use of fresh preparations. Stock solutions are said to become toxic as a result of the growth of fungus.

Chute [53] found that the use of spinal anesthesia is indicated less often in operations on the kidney than in operations on the lower part of the urinary tract; it is practically only in disease primary in the lower part of the urinary tract that the two kidneys are equally affected through back pressure. In cases of renal disease that require operation and in which inhalation anesthesia is contraindicated, local procaine hydrochloride anesthesia is used. The most definite indication for the use of spinal anesthesia in urology is the necessity for operation in a condition in which both kidneys have been rendered especially susceptible to the irritative action of inhalation anesthesia as a result of

53. Chute, A. L.: The Use of Spinal Anesthesia in Urology, J. A. M. A. **96**:88 (Jan. 10) 1931.

urinary back pressure or infection, or of a combination of the two. Prostatic obstruction is the condition most often presenting this picture. In this condition Chute most frequently uses spinal anesthesia. Perineal section for tight stricture is another indication for the use of spinal anesthesia because of the back pressure that it often causes. Spinal anesthesia is particularly indicated and desirable in operations for extravasation of urine, because of the back pressure and sepsis that follows.

Spinal anesthesia is contraindicated for nervous or mentally unstable patients or for those who are strongly prejudiced against its use. Chute rarely uses it for young persons.

In 1922 Chute reported 328 cases of prostatectomy in which spinal anesthesia was used. Since then he has used spinal anesthesia in 512 prostatectomies, mostly for the enucleation of the gland by the suprapubic route. A certain number of the glands was removed by the perineal route. In the 512 cases in which spinal anesthesia was used, 88 per cent gave satisfactory, 10 per cent fairly satisfactory, and 2 per cent unsatisfactory results. In 43 cases a little supplementary anesthesia was used. Chute did not have any immediate or remote fatalities that could be attributed to spinal anesthesia in the 1,000 cases in which it was used.

Ewell [54] stated that the use of a local anesthetic in the urethra is successful to a certain degree; it permits satisfactory cystoscopic examination and other manipulations in some cases. Cocaine is the only drug that will produce satisfactory anesthesia by topical application to the urethra; in Ewell's experience the reactions from its use have been numerous and at times disconcerting. Cystoscopic examinations and all operative procedures through the cystoscope should be made as painless as possible in order to secure better cooperation from both the patient and the physician. Caudal anesthesia produces sufficient relaxation of the bladder for complete cystoscopic examination and treatment in all types of cases. The operative procedures are painless, and the work of the operator is facilitated. It also provides safe and reliable anesthesia for perineal operations and operations on the external genitalia of men, and operations on the rectum and perineum of women. Intradural caudal anesthesia is recommended because of its simplicity and reliability; complete sacral block anesthesia can be produced by a single intradural injection, whereas by the extradural technic the introduction of a needle and anesthetic solution into the sacral canal and into several or all of the eight sacral foramina would be necessary.

54. Ewell, G. H.: Intradural Caudal Anesthesia in Urology, J. A. M. A. **96:** 91 (Jan. 10) 1931.

Because of the advantage of relaxation, intradural caudal anesthesia is of special value for prostatic punch operations.

Lundy [55] expressed the belief that sacral block anesthesia is safer than spinal anesthesia. The latter gives a greater degree of anesthesia in operations on the bladder for tumor or for diverticula than does sacral or abdominal block anesthesia, but for prostatectomy in patients who are elderly, especially if they are more than 70 years of age, sacral and abdominal block should be employed; debility is a contraindication for spinal anesthesia. It is Lundy's opinion that the technic for using crystals of procaine hydrochloride in spinal fluid is proper, and he is not satisfied with the use of lighter and inferior solutions. Ephedrine is of value in supporting the blood pressure in certain cases. Hypotonus is a definite contraindication to the use of spinal anesthesia.

Campbell [56] stated that in 1920, at Bellevue Hospital, spinal anesthesia was used in 5 cases; for the last five years it has been the routine method for all urologic operations, except when contraindicated. Spinal anesthesia has been used in about 3,000 of their urologic operations. In only 4 cases was the cause of death attributed to the spinal anesthetic. One man died eight hours after prostatectomy.

It is the practice at Bellevue Hospital to use ephedrine, allowing about twenty minutes before lumbar paracentesis puncture is made. Campbell expressed the belief that barbital hypnotics are preferable to morphine before operation. If the anesthetic is adequate pharmacologically, there is no indication for morphine and the administration of 1 grain (0.06 Gm.) of phenobarbital preoperatively will not only quiet the patient's nerves but afford the barbiturate counteraction against possible procaine poisoning. Crystals of procaine hydrochloride dissolved in spinal fluid are used; this preparation has produced satisfactory anesthesia in all types of urologic operations.

UROGRAPHY

Cumming [57] stated that a combined method of fluoroscopy and urography with the Cinex camera has given much satisfaction, with interpretations of increasing value. The securing of a complete, accurately timed series of films, showing the pelvis and ureter in all stages of emptying, will aid greatly in the making of an accurate diagnosis. Actual photographs of the phases of pelvic and ureteral activity promise a

55. Lundy, J. S.: Discussion of Papers by Bumpus, Chute and Ewell on Spinal and Sacral Anesthesia, J. A. M. A. **96**:94 (Jan. 10) 1931.

56. Campbell, M. F.: Discussion of Papers by Bumpus, Chute and Ewell on Anesthesia, J. A. M. A. **96**:94 (Jan. 10) 1931.

57. Cumming, R. E.: Urography: The Development of a New Method with Physiological Data, J. Urol. **24**:587 (Dec.) 1930.

more valuable basis than fluoroscopy for the establishment of accuracy in the interpretation of urograms.

Wesson [58] stated that for ten years he has made double pyelograms as a routine precedure, using gravity pressure, and has not had any unusual reactions. The unpopularity of double pyelography has been due to attributing to it the effects of surgical shock brought on by urethral instrumentation. Any patient who will tolerate bilateral ureteral catheterization is a subject for double pyelography, since lavage with 1 per cent silver nitrate is more irritating than with 13.5 per cent sodium iodide.

Wesson's simple apparatus for pyelography consists of an 18 inch (45 cm.) ring stand, a double buret clamp, two 25 cc. burets, 80 inches (203 cm.) of one-eighth inch (0.3 cm.) rubber tubing, two adapters and pinchcocks. The head of the table is lowered; when the column in the buret becomes stationary, the pelvis of the kidney is filled. Since only 18 inches of pressure is permitted by the apparatus, which is placed on a low stand, there should be no overinjection, and the patient should not experience pain.

Shapiro and Veseen [59] stated that with the more common use of nontoxic solutions for pyelography, there is much discussion as to whether it should be used on both sides at the same time. Among the advantages of bilateral pyelography are the time and expense saved the patient by completing the procedure at one examination. Shapiro and Veseen stated that there are also decided disadvantages, and reported 5 deaths following and directly attributable to bilateral pyelography. In 2 cases thorium nitrate was used as the pyelographic medium; in 1 case, 25 per cent sodium bromide, and in the other 2 cases, 12.5 per cent sodium iodide.

Substances that are toxic when absorbed should be distinguished from those that are not, and in making a pyelogram a solution should not be used that cannot be injected, without injury, intravenously in the same quantities and concentrations. The former opinion, that forcing the pyelographic fluid into the straight tubules was the danger in pyelography is not now believed to be the case, except when great force is used. The highest mortality and the most severe reactions seen when colloidal silver was used were in the cases in which there was evidence of systemic poisoning; hemorrhagic diathesis was common, and necropsy showed the presence of colloidal silver in distant viscera as well as in the opposite kidney. Thorium nitrate in 15 per

58. Wesson, M. B.: Interpretation of Pyelograms, J. Urol. **24**:595 (Dec.) 1930.

59. Shapiro, I. J., and Veseen, L. L.: Untoward Results in Bilateral Pyelography, J. Urol. **24**:621 (Dec.) 1930.

cent solution was next to come into favor. It casts a satisfactory shadow on the roentgenogram, and Burns found that it was only slightly toxic in experimental work. Weld, in his experimental work, found that sodium bromide had a low degree of toxicity when used either intravenously or in the pelvis of the kidney, and the 25 per cent solution cast a satisfactory shadow on the roentgen plate. Graves and Davidoff, in further experimental work with the bromide solution, found that it produced edema of the bladder and partial retention of urine in rabbits. Thrombosis of the small vessels with numerous small hemorrhages was also seen. They ascribed this irritating effect to the fact that sodium bromide in 25 per cent solution is hypertonic as compared with normal body fluids. Physiologic sodium bromide did not produce this condition. Cameron was the first to advocate the use of sodium and potassium iodide for pyelography, but because of its great toxicity it has been discontinued. He first used these salts in 17.5 per cent solution, but strengths as low as 10 per cent have been found satisfactory. Sodium iodide is isotonic in a strength of 14.56 per cent and does not injure the mucosa of the bladder or kidney.

In a case in which infection followed pyelography, the iodide solution lowered the resistance of the tissues, and gave the infection free rein. The pelvic and peripelvic blood vessels must have been the medium of transmission of the infection in order to give rise to abscesses situated solely in the kidney and perinephritic tissues.

Intravenous Pyelography.—Teposu and Jiànu [60] have used iopax for intravenous pyelography since April, 1930, with satisfactory results. Five cases in which the method was of particular value were described and illustrated with roentgenograms. One case showed symptoms of tetany during the second part of the injection, which lasted for a period of about ten minutes. Following the intravenous injection of calcium the condition returned to normal. It is the contention of the authors that since this patient normally presented hypocalcemia, there was latent tetany which was activated by the injection.

Pyeloscopy.—Hryntschak [61] stated that pyeloscopy is used in all of his cases in which a roentgen examination of the renal pelvis is indicated, but he did not consider applying it as the sole method of examining the filled renal pelvis. Pyeloscopy supplements pyelography in control of the filling process and in observation of the emptying process. By its use it is possible to ascertain whether the tip of the catheter is in proper position in the renal pelvis, whether it has been advanced

60. Teposu, E., and Jiànu, S.: Intravenous Pyelography, Cluj. med. **11**:235 (May) 1930.

61. Hryntschak, T.: Combined Pyeloscopy; Its Clinical Value and Its Technique, J. Urol. **24**:549 (Dec.) 1930.

too far in a calix or whether it has slipped down into the ureter. By direct observation during the injection, the proper quantity of fluid can be controlled, without relying on the statement of the patient. The statement of the patient regarding an approaching sense of tension frequently does not indicate the crucial moment. With pyeloscopy, the functioning of the organ in its various phases of physiologic activity can be observed.

After introducing the catheter a plain plate is taken. Then the Bucky diaphragm is removed or the patient is transferred to the roentgen table, and the tube under the table is turned on. It is important to outline the catheter clearly and to make certain of the situation of its tip. With the excursion of the diaphragm a movement of the tip of the catheter should be seen. A solution of umbrenal or of 30 per cent sodium iodide is then slowly injected, after which it is possible to ascertain accurately whether the tip of the catheter is in the proper position in the renal pelvis. If the tip is too high, only one of the calices fills. The catheter must then be withdrawn accordingly. When the renal pelvis and calices are sufficiently filled, the injection is stopped. The syringe is attached to the left ureteral catheter in order to prevent any back flow. Careful examination of the filled renal pelvis is made to determine whether all of the calices are properly filled and whether the outlines of the pelvis and calices are sharply defined. This is the proper time to establish the relative position of the renal pelvis in respect to shadows which may have been found in the plain plate, and in regard to palpable tumors in the region of the kidneys. Direct palpation of the tumor, displacement of the kidney by the palpating hand and change of the patient's position will be found useful. After a careful study of the outlines of the pelvis, the first pyelogram is taken immediately. It is important to do this in the posterio-anterior direction, as that method fixes what has been seen and makes it available for future detailed analysis. Without further injection of any fluid the ureteral catheter is slowly withdrawn. The onset of peristalsis of the ureter may easily be seen even when the catheter is still in position. The shadow of the renal pelvis then enlarges to include the upper 1 to 2.5 cm. of the ureter. The lower end of the shadow in the upper part of the ureter gradually converges to a point. At the ureteropelvic juncture contraction takes place, which forces the opaque medium in the conus down into the bladder. The formation of the conus should be considered as the normal type of initial peristalsis of the ureter. In observing the emptying of the renal pelvis it is important to note the total time consumed in the process. It is known that a normal renal pelvis ejects about 1 cc. a minute. The time required for complete emptying of the pelvis can be readily estimated from the quantity of fluid injected.

Hryntschak stated the belief that a thorough acquaintance with the screen technic of examining the renal pelvis will, in the future, be a tremendous aid in intravenous pyelography. When proper blending of these two methods has been attained, there will be available the most appropriate and informative means of investigating the anatomy and physiology of the kidneys and ureters.

DISEASE OF THE URINARY TRACT IN INFANTS

Kretschmer [62] stated that in disease of the urinary tract in infants and children the history of disturbances in the gastro-intestinal tract is of great importance, especially in cases of so-called relapsing pyelitis. Mere pelvic lavage without treatment of any gastro-intestinal lesions is not a progressive method of clearing up a renal infection. Instrumental examination should not be undertaken until there has been a careful study of the urine, preferably daily, roentgenologic examination of the urinary tract and estimation of residual urine, which should be carried out in every case in which there is a suprapubic tumor. The rule should be to study the renal function carefully before subjecting the patient to cystoscopic examination, ureteral catheterization and pyelography.

Malignant tumors of the kidney in infancy and childhood are rare. Tumors of the kidney may be classified as to point of origin as those arising in the renal capsule itself, which are rare, those of the renal pelvis, which are rare when compared with tumors of the parenchyma, and those of the renal parenchyma, which are the common malignant renal tumors. The one constant symptom is the presence of an abdominal tumor. Trauma probably plays a negligible part in the production of these tumors. Gross blood in the urine, which is common in malignant disease in adults, is uncommon in children.

Obstruction to the outflow of urine may occur anywhere along the urinary tract from the urethral orifice to the vesical neck. These lesions result in producing mechanical obstruction. The obstruction may be due to disease of the central nervous system. Fibrosis is the common cause of obstruction at the vesical orifice, although other pathologic changes occasionally are the cause. Diverticula of the bladder in children are generally associated with obstruction at the neck of the bladder. Hypertrophy of the verumontanum may produce marked obstruction to the outflow of urine. Treatment must be directed toward relieving the obstruction. Preliminary drainage of the bladder and improvement of renal function are necessary in some advanced cases. Patients with this type of obstruction have been treated by means of suprapubic

62. Kretschmer, H. L.: Diseases of the Urinary Tract in Infants and Children, Proc. Staff Meet., Mayo Clin. **5**:342 (Nov. 26) 1930.

cystostomy with the excision of a wedge-shaped piece from the fibrous neck, followed by digital dilation of the urethra. If valves are present in the posterior urethra, they may be destroyed at the same time.

Chronic renal tuberculosis is rare during infancy and childhood. The diagnosis may be facilitated by careful examination in every case in which pyuria or hematuria is present, as well as in every case in which there are persistent vesical symptoms.

Calculi in the urinary tract of children are relatively rare, and case reports are meager. When stone occurs it is usually found in the bladder. In the average case of renal and ureteral stone the syndrome tallies closely with that presented in cases of stones in adults.

It is generally recognized that the most common disease of the urinary tract in infants and children is what is called pyelitis or cystopyelitis. The pyelo-ureterogram, showing the important rôle of stasis and faulty drainage, and the frequency with which hydronephrosis and stricture of the ureter with dilatation of the ureter occurs, has helped to change Kretschmer's conception of the old clinical picture of so-called pyelitis. In this group of cases the colon bacillus is the common, but not the only, invading organism. These cases are divided into two groups: one in which the disease apparently runs a self-limited course and the patients recover with or without medical treatment and another in which there is a history of several or many recurring attacks of acute pyelitis with its symptoms of chills, fever, sweats and often great prostration. Gastro-intestinal symptoms occur occasionally. When the acute attack subsides the urine seldom clears up entirely, but should it be clear, colon bacilli are sometimes found on culture. In acute cases the treatment consists of rest in bed, the use of large quantities of fluid and careful attention to the gastro-intestinal tract. In the relapsing cases treatment depends on the underlying pathologic condition.

INFECTION OF THE URINARY TRACT

Earlam [63] stated that staphylococci are common pathogenic organisms in infections of the urinary tract, either producing an uncomplicated infection or complicating any preexisting lesion. Many staphylococci have the property of splitting urea, with the formation of ammonium carbonate. The commonest of these is *Staphylococcus albus,* certain strains of which have strong urea-splitting properties without being pathogenic in the urinary tract. Other staphylococci may be, but less frequently are, the cause of ammoniac fermentation of the urine. The staphylococci that are able to split urea do not show essential differences

63. Earlam, M. S. S.: Urea-Splitting Staphylococci in Urinary Tract Infections, Brit. J. Urol. **2**:233 (Sept.) 1930.

from those which do not have this property, with the exception that the former may possess a greater tendency to infect the urinary tract. The possession of urea-splitting properties by the infecting organism becomes of clinical significance when the infection is gross, with strong urea-splitting power, or when residual urine or urinary lithiasis is present. Treatment for infection due to urea-splitting organisms is essentially that for urinary infections in general.

CORRECTION

In the article by Dr. Bernhard Steinberg, "The Cause of Death in Acute Diffuse Peritonitis" (ARCH. SURG. **23**:145 [July] 1931), the percentage of animals in the last line on page 147 should read 100 instead of 10.

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